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TITLE: Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on
Circulating Estrogens and IGF-I in Premenopausal Women

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14. ABSTRACT This proposal entitled "Effects of moderate aerobic exercise combined with caloric restriction on circulating estrogens and IGF-1 in premenopausal women" examined the effects of exercise training combined with caloric restriction, resulting in weight loss, on two hormonal biomarkers for breast cancer i.e., circulating estrogens and insulin-like growth factor I (IGF-I). In 33 women who completed the study, exercise 4 X per wk at 79 ± 6 % of maximal heart rate combined with an 32% decrease in caloric intake over four menstrual cycles produced significant increases in aerobic capacity (27 ± 5 %), decreases in body weight loss ranging from 1-9 kg, and loss of body fat ranging from 5 to 12% of initial percent fat. Light conditioning resulted in significant gains in aerobic capacity (30 ± 5 %), but only produced a trend toward a decrease in body fat percent (-1.2%), and only a small change in body weight (-0.8 kg). Despite the highly significant changes in body composition and body weight in the exercising group, preliminary results indicate no significant changes in serum estradiol or serum estrone. IGF-I did not change significantly either, indicating that chronic exercise and dieting do not result in favorable changes in two hormonal biomarkers for breast cancer.					
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INTRODUCTION

This proposal entitled "Effects of moderate aerobic exercise combined with caloric restriction on circulating estrogens and IGF-I in premenopausal women" was designed to provide important scientific contributions with respect to the primary prevention of breast cancer in women. Specifically, this study examined potential mechanisms relating to the role of physical activity in the reduction of the risk of breast cancer by experimentally testing whether moderate aerobic exercise can reduced the levels of two hormonal biomarkers, circulating estrogens and insulin-like growth factor I (IGF-I). Since elevated levels of both of these hormones have been associated with an increased risk of breast cancer, and because exercise and weight loss has been shown to induce disturbances in menstrual cyclicity that may reduce circulating estrogens, we wished to extend previous findings from epidemiological and cross-sectional studies by performing a tightly controlled, prospective clinical study that addressed previously unanswered questions related to the role of exercise in the modulation of estrogen and IGF-I. Although previous studies have shown that negative energy balance, and not other stressful aspects of physical exercise, can modulate reproductive function and reduce circulating estrogen levels, no studies to date have determined the magnitude of energy deficit required for these changes during long-term training, and no studies have attempted to differentiate between the exercise-induced changes in ovarian versus adipose sources of circulating estrogens. Since both estradiol (ovarian) and estrone (adipose tissue) are biologically active, and because the importance of estrone as a risk factor increases with age and adiposity, it is important to consider the degree to which exercise which creates a negative energy balance affects both of these sources of circulating estrogens.

Circulating levels of IGF-I correlate with breast cancer risk, yet studies examining the responses of this hormone and its binding proteins to chronic exercise are lacking. Since IGF-I levels are very sensitive to nutritional status, previously reported stimulatory effects of exercise on IGF-I can be overridden if exercise is performed in the face of negative energy balance. In this regard, exercise that promotes weight loss can be viewed as a way to reduce levels of IGF-I, and therefore potentially reduce the risk of breast cancers. To date, no studies have addressed whether a program of moderate aerobic exercise and dietary restriction producing a negative energy balance that is carried out over a long duration will significantly alter IGF-I levels. Further, the degree to which these levels might be altered in individuals of differing initial energy stores has not been addressed.

Metabolic energy availability is an important contributing factor in the development of reproductive cancers. However, current methods for assessing energy availability, which include anthropometric measures, calculations of energy balance, evaluation of various serum and urinary biomarkers are prone to measurement error, not sensitive to alterations in energy availability, and are sometimes affected by disease states. The current project includes an introduction of a novel approach to estimating energy status by measuring metabolic hormones in plasma, insulin, IGF-I, IGFBP-1 and leptin. Recently, dried blood spot (DBS) sample collection techniques have allowed for endocrine based population studies examining a wide variety of ecological factors that contribute to variation in human reproduction. In order to use the proposed method of energy status assessment in large population-based applications, such as those addressing the role of physical activity and or diet in the risk of breast cancer, the battery of metabolic hormones that comprise the proposed method must be amenable to collection and assays. Although the DBS technique has been partially validated for some hormonal assays, it has not yet been properly validated for insulin, IGF-I, IGFBP-1 and leptin, and it is unclear whether the technique is responsive to physiological changes of these compounds. Therefore, the current work calls for the validation of the DBS sampling technique for these assays under physiological conditions.

The proposed studies will yield new and important information regarding the degree to which an exercise and diet program that results in an energy deficit will reduce the risk of breast cancer.

BODY

Study Design: The study utilized a prospective, randomized design that tested the effects of a moderate exercise program (4X/wk; 4 months) combined with moderate dietary restriction that results in an average daily energy deficit of -20%-35% kcals (Figure 1). Previously sedentary, eumenorrheic women aged 25-40 years were assigned to exercise or light conditioning groups. Initially, we had targeted both normal weight (BMI 21-25 kg/m²) and overweight (BMI 26-30 kg/m²) women to be assigned to either the Exercise (exercise 4 X epr week; 20-30% dietary restriction) or Light Conditioning groups (exercise 2X/wk; no dietary restriction) groups; 4 groups, n=15 each group. Subjects were studied for a total of six menstrual cycles, i.e., 2 control followed by 4 cycles with training and dietary restriction.

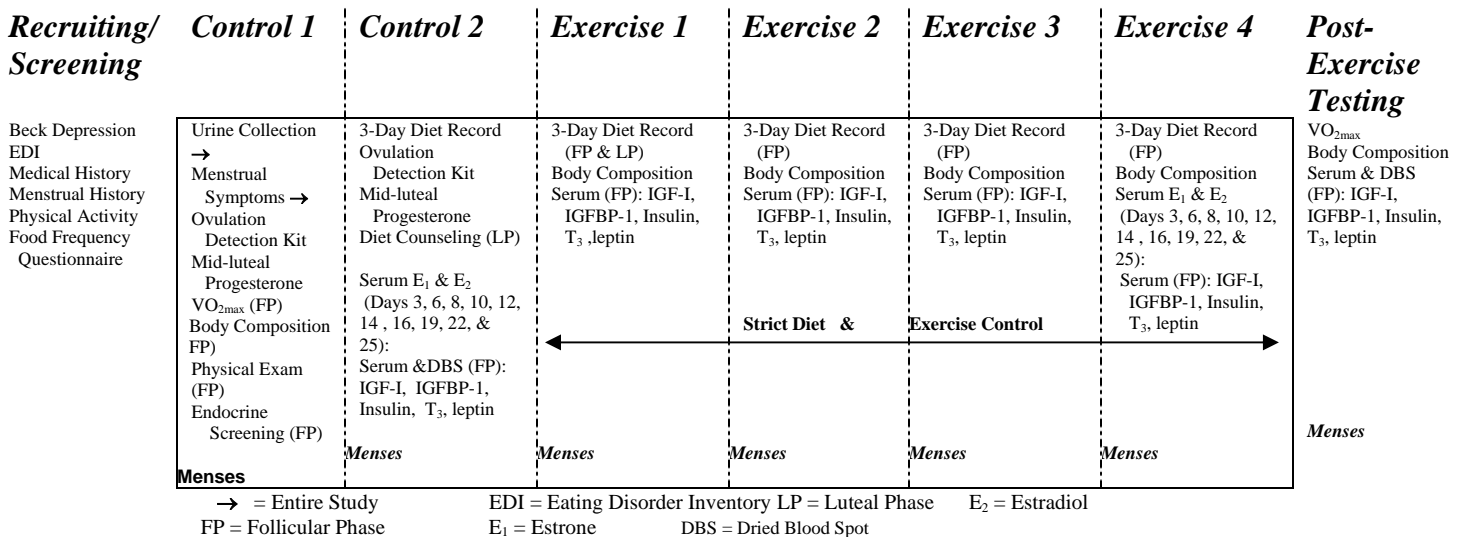


Figure 1. Study Design

Progress According to the Approved Statement of Work (2004-2005):

(See previous Annual Summary for 2003-2004)

Proposed Months 38-42, October, 2004-February, 2005:

- Requested extension for final report for this study (IDEA Award) from DAMD;
- Perform urinary LH, E1G, and PDG assays, and serum metabolic assays when final cohort is finished;
- Perform insulin, IGFBP-2, estradiol, and estrone on remaining completed subjects;
- Send completed DBS samples from completed subjects to Salimetrics
- Perform data analysis;
- Obtain results of DBS samples from Salimetrics,
- Submit abstract for ERA of HOPE Meeting in December, 2004

Actual Months 38-42, October, 2004-February, 2005:

- Extension requested and granted for final report for this study (IDEA Award); **We are unclear why another request for a Final Report was made in October of 2005.**
- Urinary assays for LH, E1G, and PdG assays from 47 subjects were performed during February – March of 2005.
- Assays for estrone, estradiol, and insulin performed on samples

- Results obtained from DBS samples sent to Salimetrics
- Data Analysis Performed
- Abstract submitted for ERA of HOPE meeting

Proposed Months 43-48, March 2005- May 2005:

- Write and submit manuscripts:

Actual Months 43-48, March 2005- May 2005; including June –October 2005

- **Manuscript #1:** In Progress: Effect of Exercise Training on Estrogen Metabolism in Premenopausal Women. Kim C. Westerlind, Jennifer Bell, Nancy I. Williams

This manuscript is in progress, and is being written in collaboration with Dr. Kim Westerlind, AMC Cancer Center, Boulder, Colorado. An increasing body of data provides evidence that being physically active reduces a woman's risk for developing breast cancer. To date, the mechanism for this reduction in risk remains unknown. The current study was designed to examine how exercise combined with caloric restriction alters circulating estradiol and estrone, and circulating concentrations of IGF-I. Another hypothesis is that exercise may exert more subtle changes in steroid hormone profiles, specifically that exercise may result in an increase in the hydroxylation of the parent estrogens through the 2-hydroxylation pathway with a concomitant decrease through the 16 OHE pathway. Higher levels of 2OHE1 have been associated with decreased breast cancer risk. In animal tumor models, increased 2OHE1 results in reduced tumorigenesis. In contrast, 16OHE1 has potent estrogenic effects and has been reported to be elevated in normal and malignant tissue from women with breast cancer. We proposed that exercise increases the ratio of 2/16 OHE1. We reasoned that this in turn might be a factor in the physical activity-mediated reduction in breast cancer risk that has been observed in epidemiological and some animal studies. We sought to examine the effect of exercise training on estrogen metabolism. We hypothesized that exercise training would result in an increase in the 2/16 ratio.

Urine samples from the mid-follicular and mid-luteal phases from each cycle from each subject in the study were sent for analysis by Dr. Westerlind. Samples were shipped on dry ice to the AMC Cancer Research Center where they were stored at -80 until all samples from a given subject were available to be assayed. The funds for these assays were awarded from a separate grant that Dr. Westerlind wrote in collaboration with Dr. Williams. Estrogen metabolite levels were measured using a commercially available competitive, solid-phase enzyme-linked immunoassay (ESTRAMET, ImmunaCare, Corp) and the ratio of 2/16 computed. The frozen urine samples were brought to room temperature before testing. Samples were diluted 1:4 prior to testing with manufacturer-supplied diluent. In urine, 2-OHE1 and 16OH are found in the glucuronide conjugate form and require removal of the sugar moiety before recognition by the monoclonal antibodies. Samples are deconjugated with β -glucuronidase and arylsulphatase, then neutralized. Samples are incubated for 3 hrs at room temperature then kinetically read every 2 min for 20 minutes using a Thermomax Microplate Reader (Molecular Devices, Sunnyvale, CA). Estrogen metabolite values were determined from a calibration curve derived from six standards with the kit (0.625 – 15.0 ng/ml). All samples, controls, and standards are assayed in triplicate and all of the samples from a given subject were batch assayed to minimize interassay variability. Any sample outside of the range of the standard curve or with a coefficient of variation greater than 10% was reassayed. In house and manufacturer-supplied controls were included in each of the assays performed. Urinary 2OHE1 and 16OHE1 were normalized to urinary creatinine concentration and expressed in ng/ml/mg creatinine. Urinary creatinine was measured in duplicate using a Diagnostic Chemicals Limited Assay (company, state). The ratio of 2/16 OHE1 was computed by dividing the absolute concentration of 2OHE1 by 16OHE1. Results were analyzed using SPSS Statistical software, version 13.0. Statistical tests included t-tests and repeated measures ANOVAs or ANCOVAs.

Preliminary results from the analyses of these samples indicate that the ratio of 2/16 was significantly higher in the exercise women (1.96) compared to the controls (1.41). This was factored into the statistical analyses. Estrogen metabolite values for the subjects overall were stable over the control and intervention periods. 2OHE1 and 16OHE were higher during the luteal phase than the follicular phase as would be expected as the concentration of the metabolites parallels the changes in estradiol during the menstrual cycle. The 2/16 ratio was not significantly different between the follicular and luteal phase for any of the months of assessment (P values ranged from 0.30 to 0.99). In order to evaluate the change in 2/16 over time, the percentage change between each of the months of the studies was calculated and graphed. Data for the 2/16 were evaluated by calculating the percent change over the course of the intervention programs. 2/16 increased linearly in the follicular phase ($p=0.004$) but did not differ between groups ($p=.91$). In the luteal phase, initial 2/16 ratios were lower in the Light Conditioning group (1.41) vs the Exercise group (1.94) ($p=0.04$). After adjusting for initial differences, significant increases over time were observed ($p<0.001$) but no difference was observed between groups ($P=0.53$). Evaluating the data further, we analyzed the relationship between a woman's initial 2/16 values in both the follicular and luteal phases and her exercise-associated changes in 2/16. Correlations between baseline follicular and luteal 2/16 ratios was $r = 0.79$. Baseline values for 2/16 were significantly associated with the percent change in the ratio over the exercise periods. Most dramatically, the 2/16 ratios in the follicular and luteal phase of the baseline month were correlated $r = -0.59$ ($p=0.002$) and $r = -0.72$ ($p<0.001$) with the total percent change (defined as the percent change between baseline and the fourth exercise month) in 2/16 luteal phase. When we divided the women into quartiles ($n=6/\text{quartile}$) based on either their baseline follicular or luteal 2/16 ratios with experimental groups combined (Tables 1 and 2), we observed a significant effect of exercise on the ratio of 2/16. Women within the lowest quartile, i.e., those with the lowest ratio of 2/16, had the largest increase in the ratio in response to exercise. Absolute estrogen metabolite values as well as percentage change over time were not associated with any change in body composition, BMI, or weight.

Table 1. Study 2: Total Percent Change in 2/16OHE1 based on baseline follicular 2/16OHE1 ratio

Quartiles 2/16 OHE1 ($n=6/\text{quartile}$)					
	1 ($X = 0.78$)	2 ($X = 1.57$)	3 ($X = 2.20$)	4 ($X = 3.18$)	SIG
% Change 2/16 Follicular phase	116 + 29% ^a	-6 + 11 %	30 + 28%	29 + 28%	P=0.007
% Change 2/16 Luteal phase	75 + 14% ^b	32 + 10%	-8 + 24%	2 + 5%	P=0.004

Overall significance determined by ANOVA with post-hoc LSD

^a significantly different than quartiles 2, 3, 4

^b significantly different than quartiles 3 and 4; NS between quartile 1 and 2 ($p=0.54$)

Table 2. Total Percent Change in 2/16OHE1 based on baseline luteal 2/16 OHE1 ratio

Quartiles 2/16 OHE1 ($n=6/\text{quartile}$)					
	1 ($X = 0.77$)	2 ($X = 1.53$)	3 ($X = 2.38$)	4 ($X = 3.16$)	SIG
% Change 2/16 Follicular phase	88 + 36%	22 + 27%	16 + 26%	43 + 18%	P=0.226
% Change 2/16 Luteal phase	70 + 17% ^a	37 + 19% ^b	3 + 10%	-9 + 22%	P=0.007

Overall significance determined by ANOVA with post-hoc LSD

^a significantly different than quartiles 2, 3, and 4

^b **significantly different than quartile 4**

In conclusion, the data suggest that women who have low 2/16 ratios may respond positively to exercise training with an increase in 2/16. Literature suggests that women with low 2/16 ratios may be at higher risk for developing breast cancer. Thus, exercise training may be of significant benefit to reducing breast cancer risk, particularly for those women at greatest risk. This manuscript is on track to be submitted in January, 2007 to *Cancer Epidemiology and Biomarker Prevention*. An abstract describing this work has been submitted for presentation at the American College of Sports Medicine, June, 2006 in Boulder, Colorado:

Estrogen Metabolism is Altered with Exercise Training Kim C. Westerlind, FACSM, Jennifer Bell, and Nancy I. Williams, FACSM. AMC Cancer Research Center, Denver, CO and Noll Laboratory, Penn State University, University Park, PA

- **Manuscript #2:** In Progress: Susceptibility to energy-related menstrual disturbances is reduced with increased age. Nancy I. Williams, Heather Leidy, Brandy Weller. Penn State University, University Park, PA. 16802.

Although energy deficiency is known to disrupt reproductive function in exercising women, no studies have examined whether the susceptibility to menstrual disturbances is altered with increased age. Therefore, the purpose of this study was to determine whether increased age is associated with reduced susceptibility to menstrual disturbances caused by chronic energy deficiency. A subset of twenty-four premenopausal women (12 young and 12 middle aged) from a larger study were matched according to the amount weight lost during a three month diet and exercise intervention. Menstrual status was assessed with daily urine samples and measurement of estrogen (E1G) and progesterone (PdG) conjugates using ELISA. The occurrence of menstrual disturbances, i.e., short luteal phases, inadequate luteal phases, oligomenorrheic cycles, and anovulatory cycles was quantified according to the number of defects/number of cycles observed. Independent samples t-tests were conducted to determine if there was a significant difference between younger and older women in the occurrence of menstrual disturbances.

The results are shown below:

	Age	Gynecologic Age	Occurrence of Defects	Weight Loss	% Energy Deficit
Young (n=12)	20.2 ± 1.9	8.0 ± 2.0	1.92 ± 2.02	-4.6 ± 1.4	-20.0 ± 17.2
Middle Aged (n=12)	33.5 ± 4.2	21.4 ± 4.8	0.58 ± 0.90	-4.6 ± 1.4	-37.7 ± 11.3
	p<0.00*	p<0.00*	p<0.05*	p<0.95	p<0.05*

In conclusion, older age was associated with significantly fewer disturbances in response to weight loss resulting from a diet and exercise intervention. These results suggest that factor(s) associated with increased age confer protection against menstrual disturbances caused by energy deficiency. An abstract describing this work has been submitted for presentation at the American College of Sports Medicine, June, 2006 in Boulder, Colorado:

Susceptibility to energy-related menstrual disturbances is reduced with increased age. Brandy Weller, Ann Albert, Matthew Johnson, Nancy Williams, Penn State University, University Park, PA 16802

Report of Final Results:

Subject Recruitment:

Over the three years in which the study took place, 572 contacts through phone or email were made with women interested in the study. Of those 572 women, 85 signed informed consents for the study, 52 were excluded from the study at various time points for the following reasons: 10 for medical reasons, 17 because of time constraints or other personal reasons, 3 became pregnant during the study, 1 had abnormal prolactin levels, 6 exceeded limits for body composition or body weight, 2 dropped out because they were not able to receive financial compensation due to visa restrictions, 11 had existing menstrual abnormalities, and 2 were asked to leave because of non-compliance. There were 33 women who completed the study.

Table 1. Initial Subject Characteristics

		Age (yrs)	Weight (kg)	Height (cm)	BMI (kg/m ²)	Body Fat (%)	VO ₂ Max (ml/kg/min)
Light Conditioning (n = 16)	Mean	33.69	65.21	163.36	24.61	34.35	29.31
	Std Deviation	3.66	5.46	6.51	3.19	5.17	4.03
Exercise (n=31)	Mean	31.90	64.84	163.44	24.29	32.73	31.66
	Std Deviation	4.13	9.70	6.10	3.32	5.41	6.33

Compliance

- Began Study (n=47)
- Drop Outs (n=14): Light Conditioning = 7, Exercise = 7, (no differences between drop-outs and finishers in age, weight, BMI, body fat %, or VO_{2max})

Table 2. Descriptive Characteristics of the Completed Subjects

VARIABLE	OVERALL (n=33)	Light Conditioning (n=9)	Exercise (n=24)	SIG
Age (yrs)	32.4 + 0.8	35 + 1.0	31.5 + 0.9	P=0.049
Height (cm)	164.0 + 1.1	164.8 + 2.5	163.7 + 1.3	P=0.663
Weight (kg)	64.1 + 1.4	64.5 + 1.9	63.3 + 1.8	P=0.728
BMI	23.7+ 0.5	23.9 + 1.3	23.6 + 0.6	P=0.811
Body Fat (%)	32.3 + 0.9	34.3 + 1.8	31.6 + 1.0	P=0.192
VO ₂ max (ml/kg/min)	31.7 + 1.0	28.8 + 1.1	32.7 + 1.2	P=0.027

Data are presented as Mean + SE. Significance determined by t-test between Control and Exercise groups.

Dietary Intake During the Intervention:

The target macronutrient composition for all subjects during the intervention was 55% carbohydrate, 30% fat, and 15% protein. Using the average total daily caloric intake from the each subject's three day diet log, in combination with the Harris Benedict equation as adjusted for daily physical activity (Harris 1919), an estimate of the eucaloric (weight maintenance) energy needs of each subject were calculated. In order to promote weight loss, this level of dietary intake was reduced by 20-40 % for exercising subjects, and this new level was their target daily caloric intake throughout the intervention. For light conditioning subjects, the target level of daily dietary intake during the intervention remained that which represented their eucaloric energy needs. Prior to the intervention the GCRC dietician taught all subjects how to use the food exchange system (American Diabetes Association, 2003 Edition, Chicago, IL) to obtain their targeted caloric intake, and the targeted macronutrient composition. Subjects kept track of their daily food exchanges by recording them on monitoring forms for seven days at a time, every two weeks. Estimates of daily caloric intake from food exchange monitoring sheets were determined using Dietician's Assistant v. 2.99 (Compu-Cal Inc., Olympia, WA). Once per menstrual cycle during the intervention subjects also completed a 3 day diet log. Total calories and macronutrient content was determined using Nutritionist Pro (First Data Bank, Indianapolis, IN). If difficulties arose with subjects meeting their targeted caloric intake, the dietician counseled on how to overcome these challenges. If subjects in the Light Conditioning group were experiencing weight changes, or if subjects in the Exercise group were not losing weight, appropriate changes to the target caloric intake were made. Dietary counseling sessions for both Light Conditioning and Exercise groups included discussion of food education modules including Shopping Tips, Low Fat/Low Calorie food, Food Preparation, Dining Out, Iron, Calcium, Fiber, and Vitamins in Food.

Exercise Training During the Intervention

Subjects in both groups attended supervised exercise sessions in the training room in Noll Laboratory that were monitored by a Head Trainer and several personal trainers who had experience in fitness assessment and personal training. Workouts for the exercise group were four times per week and consisted of a 5 minute warm-up followed by approximately 40-90 min of aerobic activity at a heart rate 60-90% (average $79 \pm 0.7/6.0\%$ (sem/SD)) of the maximal heart rate (obtained from the VO_2 max test achieved during exercise sessions), followed by a 10 min cool-down. Modes of aerobic activity included treadmill walking, stationary cycling, and stair stepping. Average attendance for subjects in the Exercise group was $96 \pm 0.9/4.6$ (sem/sd) % of the total workouts. The duration of exercise for the Exercise group was equal in minutes to that required to expend a target amount of calories, determined to be 20% of the subjects' eucaloric intake. For example, if the pre-determined eucaloric intake was 2000 calories, then this subject's exercise calorie target would be 400 calories. The total amount of calories expended during each exercise session was measured using the OwnCal feature on the Polar S610 heart rate monitor (Polar Electro Oy, Kempele, Finland). Throughout the study the heart rate monitors were continually reinitialized with the most recent values of weight, maximum heart rate, maximal aerobic capacity, and age.

Light conditioning subjects exercised 2 times per week; sessions were comprised of $36 \pm 2.9/8.3$ (sem/sd) minutes of aerobic activity at $77 \pm 0.8/2.3\%$ (sem/sd) of maximum heart rate, and 10 minutes of light stretching and calisthenics. Compliance to these sessions was 94 %. These sessions were designed to provide a sufficient training stimulus for subjects to see some improvement in aerobic capacity and strength and flexibility, but not to expend a significant amount of calories such that weight loss would be observed. Earlier attempts at recruiting subjects who would agree to be randomized to a non-exercising control group were unsuccessful.

Results

Descriptive characteristics for completed subjects are presented in **Table 2**. No differences were observed in any of the parameters after women were randomized to Light Conditioning versus the Exercise groups with the exception of age ($P= 0.049$; independent t-test). Light Conditioning women were significantly older when compared to the exercise women.

The effects of the intervention on body composition, body weight, and fitness are shown in **Table X**. In general significant improvements were observed in all variables over the course of the intervention, with the exception of no change in fat free mass. Significant group interactions were observed for all variables where significant changes occurred over time, except $\text{VO}_{2\text{max}}$, indicating that although changes were favorable in both groups, the Exercise group exhibited significantly greater gains as a result of the intervention. Average percent changes from baseline for $\text{VO}_{2\text{max}}$ for Light Conditioning and Exercise groups respectively were $+30 \pm 5\%$, and $+27 \pm 5\%$. Average percent changes from baseline for percent body fat for Light Conditioning and Exercise groups respectively were $-3.8 \pm 1.7\%$, and $-15 \pm 2.3\%$. Light Conditioning subjects lost $1.2 \pm 0.6\%$ of their initial body weight, while Exercise subjects lost $6.0 \pm 0.9\%$. Daily caloric intake from the average of three day diet logs recorded during the baseline period, and during the fourth menstrual cycle exhibited a significant decrease over time ($P < 0.001$), and this difference varied between the Light Conditioning and Exercise groups (interaction effect $P = 0.004$) such that the Exercise group experienced a 32% decrease and the Light Conditioning group experienced an 8% decrease. Average macronutrient content across the intervention was not different between groups with the exception of the percent of daily calories derived from fat. Light Conditioning subjects consumed $34.8 \pm 4.5\%$ fat versus the Exercisers who consumed $27.5 \pm 5.2\%$ ($P = 0.035$; one – way anova on average 3 day diet macronutrients for Exercise 1, Exercise 2, and Exercise 3, and Exercise 4). The overall macronutrient distribution for both groups during the intervention was $55 \pm 1.2\%$ carbohydrate, $18.7 \pm 0.7\%$ protein, $29.1 \pm 1.3\%$ Fat, and $6.5 \pm 0.8\%$ alcohol.

When serum measurements of estradiol and estrone are examined across Control Cycle 2 ($n=10$ measurements per subject), and Exercise 4 cycles ($n=10$ measurements per subject) are averaged, and then compared with paired samples T-tests, no differences are observed in either the light conditioning or exercising groups, despite the loss of body fat. A composite graph of these changes, depicted according to cycle day are depicted in Figures 1 and 2. A representative depiction of the changes in both serum estrone and estradiol and urinary E1G in one subject is depicted in Figure 3.

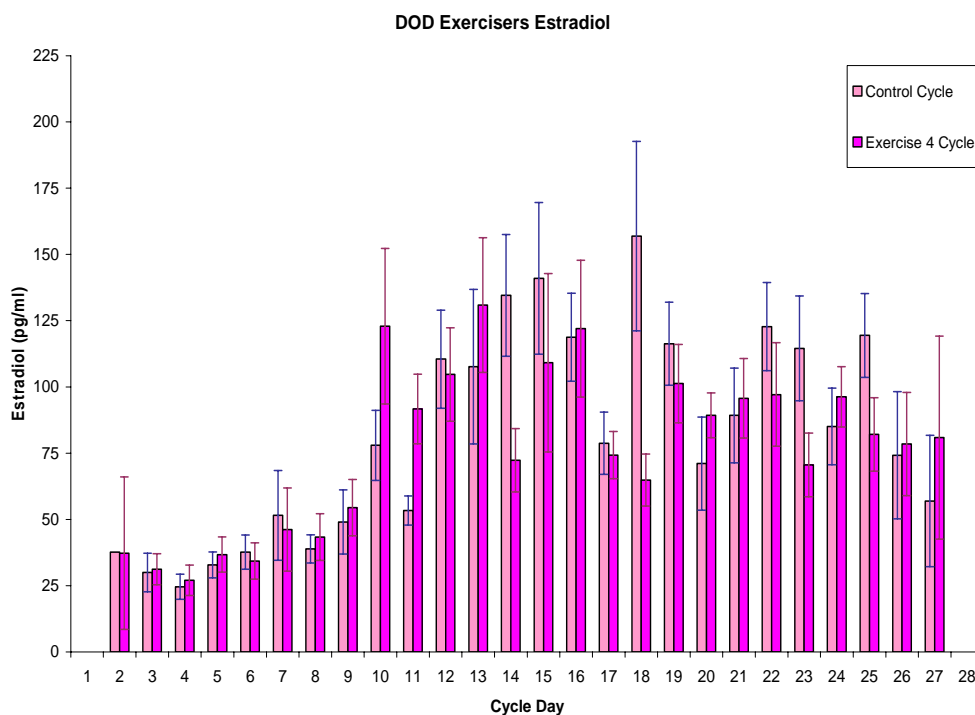


Figure 1. Composite graph of estradiol measurements from Control Cycle 2 (Pre) and Exercise 4 (Post) cycles in Exercising Subjects.

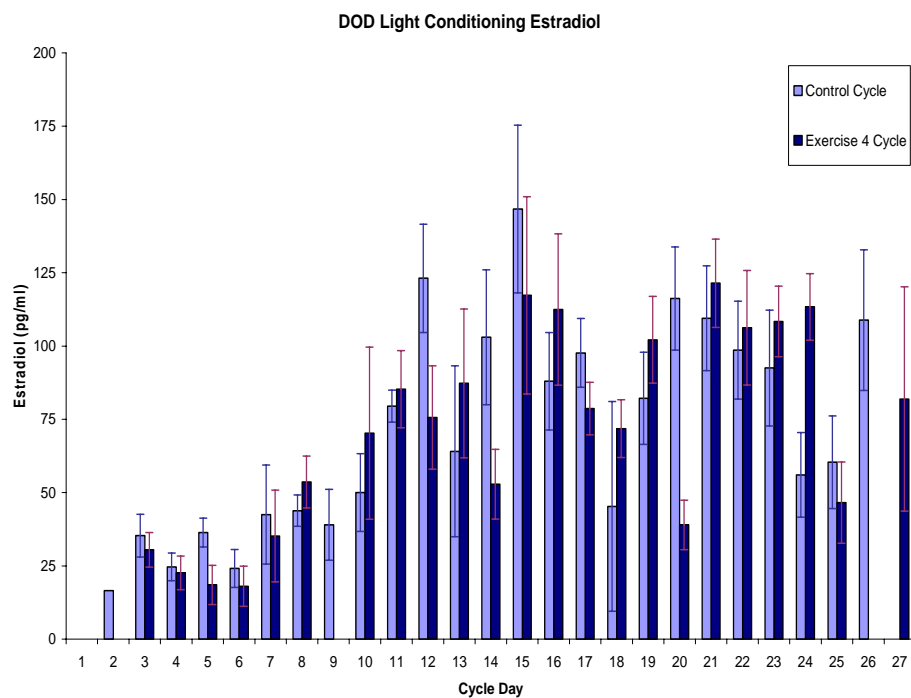


Figure 2. Composite graph of estradiol measurements from Control Cycle 2 (Pre) and Exercise 4 (Post) cycles in Light Conditioning Subjects

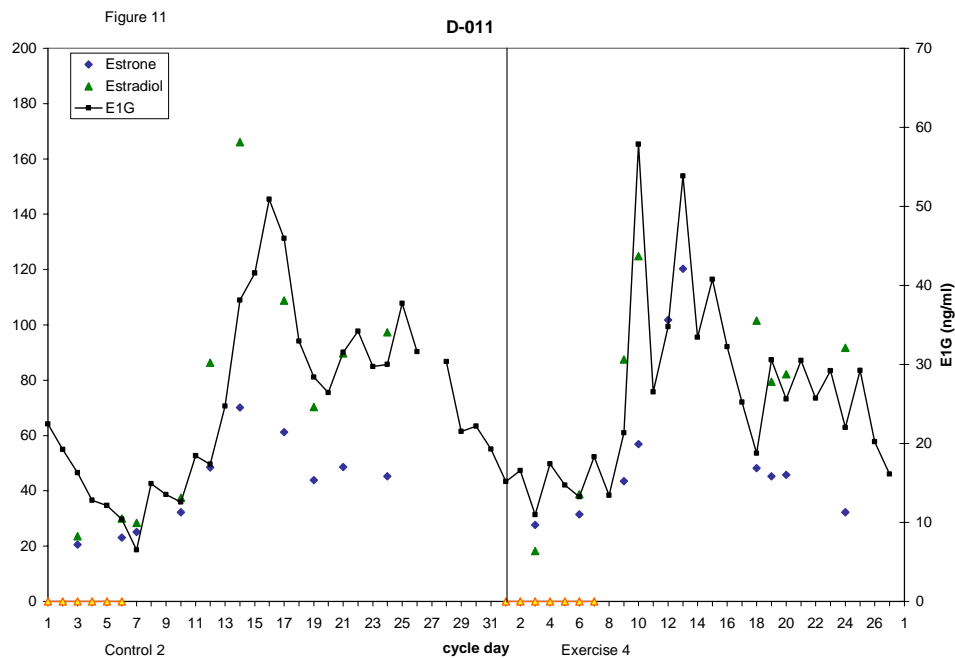


Figure 3. Representative example of a single subject's urinary (E1G) and serum estrogens (estrone and estradiol) before (Control 2) and after (Exercise 4) exercise training combined with caloric restriction.

Changes in Circulating IGF-I. During Exercise Combined with Diet Intervention:

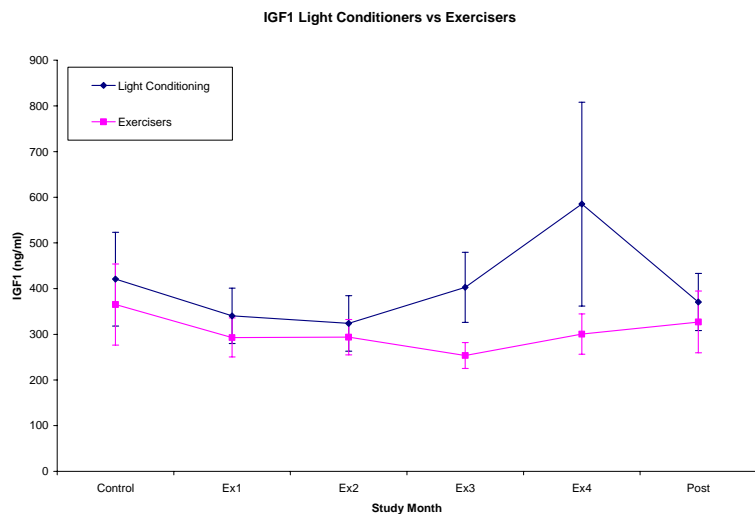


Figure 4. IGF-1 does not decline despite significant fat and weight loss in Exercise or Light Conditioning

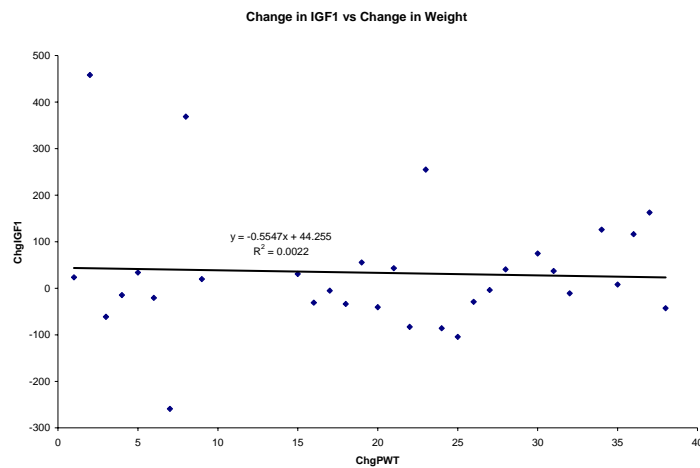


Figure 5 , and there is no correlation between change in body weight and change in IGF-1 from pre to post.

Results for Dried Blood Spot Samples:

Example results for leptin DBS samples are illustrated below. In comparison to the simultaneous venipuncture measurement of leptin as assayed in our laboratory, a significant correlation exists ($P < 0.05$; Pearson Correlation) (Table 3, and Figure 4)

Table 3 . Correlation between serum and DBS sample for leptin

		Av Control Month Leptin (ng/ml)	PreLeptinBlood Spot(ng/ml)
Av Control Month Leptin (ng/ml)	Pearson Correlation	1	.677(*)
	Sig. (2-tailed)	.	.011
	N	36	13
PreLeptinBloodSpot (ng/ml)	Pearson Correlation	.677(*)	1
	Sig. (2-tailed)	.011	.
	N	13	13

* Correlation is significant at the 0.05 level (2-tailed).

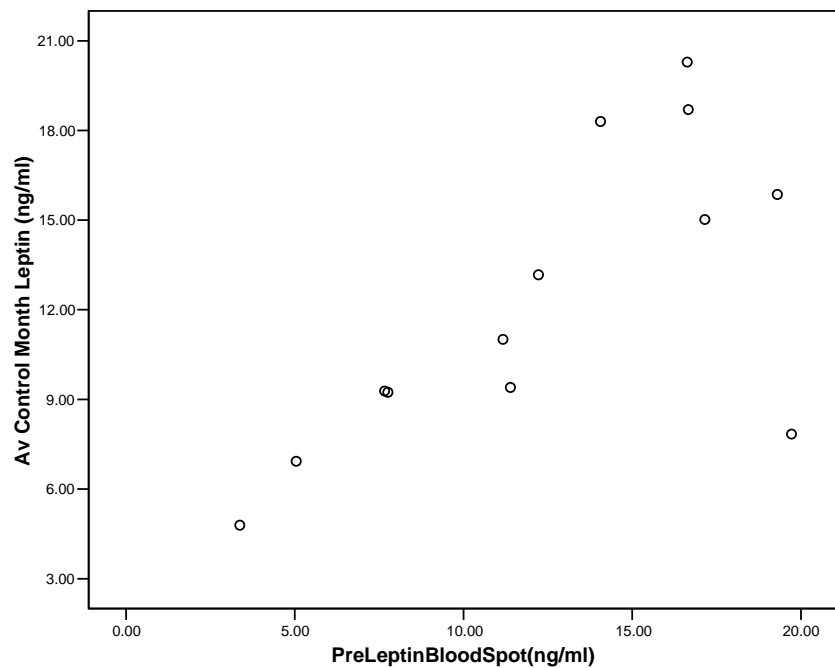


Figure 4. Scatterplot of leptin DBS vs venipuncture results

KEY RESEARCH ACCOMPLISHMENTS

Thus far:

Two Abstracts Submitted to 2006 Annual Meeting of the American College of Sports Medicine (listed above):

- 1) Estrogen Metabolism is Altered with Exercise Training** Kim C. Westerlind, FACSM, Jennifer Bell, and Nancy I. Williams, FACSM. AMC Cancer Research Center, Denver, CO and Noll Laboratory, Penn State University, University Park, PA 16802
- 2) Susceptibility to energy-related menstrual disturbances is reduced with increased age.** Brandy Weller, Ann Albert, Matthew Johnson, Nancy Williams, Penn State University, University Park, PA 16802

Manuscripts in Progress from DAMD Funding:

- 1) Effect of Exercise Training on Estrogen Metabolism in Premenopausal Women.** Kim C. Westerlind, Jennifer Bell, Nancy I. Williams

This manuscript is drafted and will be submitted in January, 2006.

- 2) Susceptibility to energy-related menstrual disturbances is reduced with increased age.** Nancy I. Williams, Kelly Dougherty, Brandy Weller, Ann Albert. Penn State University, University Park, PA 16802

This manuscript is drafted and will be submitted in February, 2006.

- 3) Effects of Exercise Combined with Caloric Restriction on Circulating Estradiol and Menstrual Cyclicity in Premenopausal Women.** Nancy I. Williams, Brian Frye, Kelly Dougherty

Methods and Results have been written.

- 4) Effects of Exercise Combined with Caloric Restriction on Circulating IGF-1.** Nancy I. Williams, Heather Leidy

Methods and Results have been written.

REPORTABLE OUTCOMES (2001-2005)

Funding Applied for and Received Based on Work Supported by this Award:

- 1. PR054531**
United States Department of Defense CDMRP Program

10/05-10/09

“Increased Caloric Intake to Reverse Energy Deficiency in Exercising Women: Impact on Bone & Menstrual Cyclicity”

This study investigates the effects of increasing caloric intake in exercising women with reduced bone mass and amenorrhea on menstrual and bone health status.

Role: Co-Principal Investigator (With MJ De Souza)

2. Cancer Research and Prevention Foundation

1/04-12/05
\$76,865 0%

“Exercise and Estrogen Metabolism: Implications for Breast Cancer Prevention”

The major goal is to test the hypothesis that a diet and exercise intervention produces favorable alterations in the ratio of key catechol estrogens that are associated with a reduced risk of breast cancer.

Role: Co-Investigator (PI is Kim Westerlind, AMC Cancer Research Center, Denver, CO)

Pending Funding Applied for and Received Based on Work Supported by this Award:

1. National Institutes of Health (NIH)

4/1/05- 3/31/09
\$856,295 15%

“Antioxidant Status, Diet and Early Pregnancy”

Role: Co-Investigator (PI is Terry Hartmen, Dept. Nutrition, Penn State)

2. National Institutes of Health (NIH) 1 RO1 HD39245-01 7/1/05-6/30/09 20%
\$ 2,020,090

“Bioenergetics of Exercise-Induced Menstrual Disturbances”

Role: Principal Investigator

3. National Athletic Training Association Research Grant 1/1/06-12/31/06
\$89,113

“Reversing Energy Deficiency in Amenorrheic Athletes: Effects on Bone Turnover and Physical Performance”

Role: Principal Investigator

Student Training:

The following individuals have been supported in Dr. Williams' Laboratory during the funding period covered by DAMD17-01-1-0360:

Masters Students

- 2002 Megan Senior "Screening for Subclinical Eating Disorders in Female Athletes: The Use of an Indirect Interview Technique " (Nutrition)
- 2004 Michael Perry " Effects of chemotherapy followed by exercise training on reproductive status and stress hormones in breast cancer patients" (Kinesiology)
- 2004 Kelly Dougherty "No relation between leptin and exercise-associated reproductive disturbances in healthy normal weight young women" (Kinesiology)
- 2004 Brian Frye "Predictors of weight loss in a diet and exercise intervention in young women" (Kinesiology)
- 2005 Sarah Giambuzzi (Kinesiology – In Progress)
- 2005 Jennifer Ward (Physiology- In Progress)

Doctoral Students

- 2004 Heather Leidy "Role of ghrelin in energy homeostasis"(Physiology)
- 2005 Jennifer Bell (In progress, Physiology)
- 2005 Brandy Weller (In progress, Kinesiology)

MANUSCRIPTS DURING THE ENTIRE PERIOD OF SUPPORT BY DAMD17-01-1-0360 (2001-2005)

(TOTAL 15 PUBLISHED, 3 IN REVIEW, 5 IN PROGRESS)

1. **Williams, N.I.**, Caston-Balderrama, A.L. Helmreich, D.L., Parfitt, D.B., Nosbisch C, Cameron, J.L. Longitudinal changes in reproductive hormones and menstrual cyclicity in cynomolgus monkeys during strenuous exercise training: rapid transition to exercise-induced amenorrhea *Endocrinology* 142: 2381-2389, 2001
2. **Williams N.I.**, DL Helmreich DL, DB Parfitt, Caston-Balderrama AL, JL Cameron. Evidence for a causal role of low energy availability in the induction of menstrual cycle disturbances during strenuous exercise training. *J Clin Endocrinol Metab* 86: 5184-5193, 2001
3. Miles MP, Mackinnon LT, Grove DS, **Williams N.I.**, Bush JA, Marx JO, Kraemer WJ, Mastro AM. 2002 The relationship of natural killer cell counts, perforin mRNA and CD2 expression to post-exercise natural killer cell activity in humans. *Acta Physiol Scand* 174: 1-9.
4. McConnell HJ, O'Connor KA, Brindle E, **Williams, N.I.** 2002 Assessing reproductive function in exercising women: validity of ovulation detection algorithms. *Med. Sci. Sports Exerc* 34(11): 1836-1844
5. Whipple TJ, Petit Moira, Sharkey N, Demers L, **Williams N.I.** 2002 Leptin and the skeleton. *Clin. Endocrinol.* 57: 701-711.
6. **Williams, N.I.**, Experimental disruptions of the menstrual cycle: Lessons from long-term prospective studies. *Med Sci Sports Exerc* 35 (8): 1564-1572, 2003.
7. De Souza, M.J.,H. McConnell, E. O'Donnell, B. Lasley, and **Williams N.I.** Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*J Clin Endocrinol Metab.* Jul;89(7):3536-42, 2004.
8. McConnell HJ, Gardner JK, Frye BR, Snook ML, Schuchert MK, Richard EL, and **Williams N.I.** Circulating ghrelin is sensitive to changes in body weight during a diet and exercise program in normal weight young women (Special edition: *J Clin Endocrinol Metab.* Jun; 89(6):2659-64, 2004.
9. De Souza MJ, and **Williams N.I.** Physiological Aspects and Clinical Sequelae of Energy Deficiency and Hypoestrogenism in Exercising Women (*Hum Reprod Update*) Sep-Oct;10(5):433-48, 2004
10. Whipple TJ, Le BH, Demers LM, Churchill VM, Petit MA, Sharkey N, **Williams N.I.** Acute effects of moderate intensity resistance exercise on bone cell activity. *Int J Sports Med* 2004 Oct. 25 (7): 496-501.
11. De Souza MJ, **Williams N.I.** Beyond Hypoestrogenism in Amenorrheic Athletes: Energy Deficiency As a Contributing Factor for Bone Loss. *Curr Sports Med Rep.* 2005 Feb;4(1):38-44.

12. **Williams, NI** and De Souza, MJ. "Exercise-associated menstrual cycle disturbances: practical and clinical considerations", in "The Endocrine System in Sports and Exercise" as part of the series "The Encyclopedia of Sports Medicine" an International Olympic Committee Medical Commission Publication in collaboration with the International Federation of Sports Medicine. Kraemer WJ, Rogol AD, eds. Blackwell Publishing, Malden, MA, Chp 20, pp 261-278, 2005
13. Hutnick NA, **Williams NI**, Kraemer WJ, Orsega- Smith E, Dixon RH, Bleznak AD, Mastro AM. Exercise and Lymphocyte Activation following Chemotherapy for Breast Cancer Med Sci Sports Exerc. Nov;37(11):1827-1835, 2005.
14. Hertel J, **Williams NI**, Kramer LC, Leidy HJ, Putukian M. Neuromuscular performance and knee laxity do not change across the menstrual cycle of female athletes. (In Press, Knee Surgery, Sports Traumatology, and Arthroscopy, 2005)
15. **Williams NI**, Leidy HJ. Food Attitudes in Female Athletes: Association with Menstrual Cycle Length (In Press, Journal of Sport Sciences, 2005)

MANUSCRIPTS IN REVIEW

1. Leidy HJ, **Williams NI**. Meal energy content affects the meal-related pattern of ghrelin but has no effect on the nocturnal pattern in normal weight, healthy young women (In Review, Hormone and Metabolic Research)
2. De Souza MJ, Hontscharuk R, Olmsted M, Burke, T, Kerr, G, and **Williams NI**. Drive for thinness is a strong predictor of energy deficiency in exercising women (In Review, Physiology and Behavior)
3. **Leidy HJ**, Frye BR, Dougherty, K, Duke KM, Albert AE, Snook ML, **Williams NI**. The Meal Related Pattern and Diurnal Rhythm of Ghrelin are Elevated Following an Energy Deficit-imposing Diet and Exercise Intervention (In Review)

MANUSCRIPTS IN PROGRESS

1. **Williams, N.I.** , Berga S.L., and Cameron, J.L. Synergistic effects of multiple stressors on menstrual cyclicity in cynomolgus monkeys. (Written, In review by co-authors; To be submitted to Journal of Clinical Investigation)
2. Westerlind KC, Bell J, **Williams, NI**. Effect of Exercise Training on Estrogen Metabolism in Premenopausal Women. (Written, In review by co-authors: To be submitted to Cancer Epidemiology and Biomarker Prevention)
- 3) **Susceptibility to energy-related menstrual disturbances is reduced with increased age.** Nancy I. Williams, Kelly Dougherty, Brandy Weller, Ann Albert. Penn State University, University Park, PA 16802

This manuscript is drafted and will be submitted in February, 2006.

- 4) **Effects of Exercise Combined with Caloric Restriction on Circulating Estradiol and Menstrual Cyclicity in Premenopausal Women.** Nancy I. Williams, Brian Frye, Kelly Dougherty

Methods and Results have been written.

- 5) **Effects of Exercise Combined with Caloric Restriction on Circulating IGF-1.** Nancy I. Williams, Heather Leidy

Methods and Results have been written.

ABSTRACTS DURING THE ENTIRE PERIOD OF SUPPORT BY DAMD17-01-1-0360 (2001-2005)

(TOTAL = 27)

- Mastro AM, **Williams NI**, Kraemer WJ, Orsega-Smith EM, Perry MD, Dixon RH, Bleznak AD, Underwood J. Exercise, quality of life, and the recovery of CD4 (+) lymphocytes following chemotherapy for breast cancer *Proceedings of the American Association for Cancer Research 92nd Annual Meeting*, New Orleans, LA , 42 : 331, March 24-28, 2001
- Perry MD, Mastro AM, Orsega-Smith E, Miles MP, Kraemer WJ, **Williams NI**. Exercise training and immune function following chemotherapy for breast cancer. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001
- Orsega-Smith E, **Williams NI** (FACSM), Perry MD, Mastro AM, Kraemer WJ, Bleznak A, Dixon R, Underwood J. Fatigue, quality of life and physical function after chemotherapy for breast cancer. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001
- Galucci, AN, **Williams NI**. Physiological indicators of psychological stress prior to competitive exercise. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001
- McConnell HJ, O'Connor KA, Brindle E, **Williams, NI**. Assessing reproductive function in exercising women: validity of ovulation detection algorithms. *Proceedings of the Endocrine Society Annual Meeting*, Abstract #P2-408, 2001
- Senior MK, **Williams NI**, McConnell HJ, Clark KC. Screening for subclinical eating disorders in female athletes: validation of an indirect interview technique. (*Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001*).
- McConnell HJ, **Williams NI**, O'Connor KA, Clark KL, Putukian M. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up clinical and physiological studies. (*Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001*).
- Mastro AM, **Williams NI**, Ford J, Fuener K, Orsega-Smith E, Kraemer WJ, Bleznak AD, Dixon RH, Underwood J, Miles M, Wagner K. IL-6 and interferon-gamma levels following chemotherapy for breast cancer. *Proceedings of the American Association for Cancer Research Annual Meeting*, San Francisco, CA, April 6-10, 2002
- Hertel J, **Williams NI**, Gribble PA, McConnell HJ, DiPasquale AA, Putukian M. Changes in risk factors of ACL injuries across the menstrual cycle: A pilot study. *Proceedings of the American College of Sports Medicine Annual Meeting*, St. Louis, MO, May 29-June 1, 2002
- Williams NI**, McConnell HM, Gardner JK, Albert AC, Cameron JL. Lifestyle factors such as exercise, caloric intake, and psychological stress: relationship to reproductive hormones and possibly the risk of breast cancer. *Era of Hope* meeting, Department of Defense Breast Cancer Research Program, Orlando, FL, September 25-28, 2002

Dougherty, K., Galucci AN, McConnell HJ, **Williams NI**. Cortisol and testosterone levels prior to competitive exercise. *Proceedings of the American College of Sports Medicine Annual Meeting* , San Francisco, May 28-June 1, 2003, *Med. Sci. Sports Exerc.* 35 (5), p. S1837, 2003.

Williams NI, McConnell HJ, Gardner JK, Cameron JL, Schuchert MK, Richard EL, Snook ML. Susceptibility of menstrual cycle to various stressors: correlation with baseline luteal progesterone levels. *Proceedings of the American College of Sports Medicine Annual Meeting* , San Francisco, May 28-June 1, 2003, *Med. Sci. Sports Exerc.* 35 (5), p. S12, 2003.

McConnell HJ, Schuchert MK, Gardner JK, Frye BR, **Williams NI**. Basal Ghrelin is sensitive to changes in body weight during a controlled diet and exercise program in normal weight young women. (Presented at the 2003 Endocrine Society Meeting, Philadelphia, PA, June 2003).

Whipple TJ, Le, B., Demers, L., Petit M.A., Sharkey N. **Williams, NI**. Acute Effects of Moderate Intensity Resistance Exercise on Bone Cell Activity. (Presented at Association for Bone and Mineral Research Meeting, 2003).

J K Gardner, H J McConnell, B R Frye, K A Dougherty, T S Parrott, E L Richard, M L Snook, M Schukert, **Williams, NI**. Validation of an Improved Method to Estimate Energy Requirements in College-aged Women: The PERK method (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S79, 2004)

K Dougherty , H J McConnell, J Gardner, B Frye, E Richard, M Snook, M Schucert, A Albert, T Parrott and **Williams, NI**. Effects of Diet and Exercise on Leptin Levels In Women: Dependence on Body Composition Changes (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S80, 2004)

Williams, NI, HJ McConnell, JK Gardner, BR Frye, EL Richard, ML Snook, KL Dougherty, TS Parrott, A Albert, M. Schukert. Exercise-associated menstrual disturbances: dependence on daily energy deficit, not body composition or body weight changes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.

De Souza, M.J., E. O'Donnell, R. Hontscharuk, T. Burke, J. Goodman, **Williams, NI**. Diagnosis of Osteopenia May Indicate the Presence of Increased Cardiovascular Risk in Female Athletes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.

R. Hontscharuk, E. O'Donnell, **Williams, NI** T. Burke, M.J. De Souza. Dietary Cognitive Restraint: A Marker for Altered Energy Homeostasis and Menstrual Disturbances in Athletic Women (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S33, 2004.

McConnell, H., **Williams, NI**, E. O'Donnell, B. Lasley, M.J. De Souza. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004)

De Souza MJ, Lee D, Burke T, Hontscharuk R, O'Donnell E, Williams NI. Metabolic Adjustments to Maintain Energy Balance in Amenorrheic Exercising Women Indicate Chronic Energy Deficiency. (Abstract # P3-568, Proceedings of Endocrine Society, San Diego, CA, 2005) p. 684.

Williams NI. Leidy HJ, Legro R, Demers L, Gardner J, Frye B, Dougherty K, Albert A, Parrott T, De Souza MJ. Predictors of Menstrual Disturbances in Exercising Women. (Abstract # P3-569, Proceedings of Endocrine Society, San Diego, CA, 2005) p. 684.

Williams NI, Albert AC, Parrott TS, Leidy HJ, Frye B, Snook M, Duke, KA, Richard EL, Gardner JK. Effects of caloric restriction combined with moderate aerobic exercise on circulating estrogens and IGF-I in premenopausal women. (Abstract presented at 2005 Era of Hope Breast Cancer Research Meeting, Philadelphia, PA, June, 2005)

A.M. Mastro, N.A. Hutnick, **N.I. Williams**, W.J. Kraemer, E. Orsega-Smith, R.H.Dixon, A.D. Bleznak. The use of exercise to increase lymphocyte activation following chemotherapy for breast cancer. (Abstract presented at 2005 Era of Hope Breast Cancer Research Meeting, Philadelphia, PA, June, 2005)

Kim C. Westerlind, Jennifer Bell, and **Nancy I. Williams**, Estrogen Metabolism is Altered with Exercise Training (Submitted for presentation at 2006 American College of Sports Medicine Meeting, Denver, Colorado, 2006)

Brandy Weller, Ann Albert, Matthew Johnson, and **Nancy I. Williams** Susceptibility to energy-related menstrual disturbances is reduced with increased age. (Submitted for presentation at 2006 American College of Sports Medicine Meeting, Denver, Colorado, 2006)

Jennifer L. Scheid, **Nancy I. Williams**, Sarah L. West, Tanya G. Burke, Mary Jane De Souza. Bone Resorption Is Increased In Premenopausal Exercising Women With Osteopenia (Submitted for presentation at 2006 International Osteoporosis Federation, June 2006, Toronto, Ontario, Canada)

INVITED PRESENTATIONS DURING THE ENTIRE PERIOD OF SUPPORT BY DAMD17-01-1-0360 (2001-2005)

(TOTAL = 17)

"Low Energy Availability and the Menstrual Cycle: Clinical and Physiological Implications" *Society for the Study of the Menstrual Cycle, Bi-Annual meeting*, June, 2001, Hartford Connecticut

"Physiological Connections Between Factors of the Female Athlete Triad" *Penn State Athletic Training Conference*", April 12, 2002, Penn State University, University Park, PA

"Exercise and Women's Health: Lessons from the Female Athlete Triad", Department of Health and Exercise Science, April 25, 2002, *Wake Forest University*, Winston-Salem, NC

"Subclinical Eating Disorders and Menstrual Cycle Irregularities in Female Athletes" *Eating Disorders on Campus, The Institutional Response*, June 7, 2002, Eighth Annual Conference, Penn Stater Conference Center Hotel, Penn State University, University Park, PA

"Effects of Exercise on the Menstrual Cycle: Physiological mechanisms and practical considerations" February, 2003, *School of Kinesiology and Health Science*, York University, Ontario, Canada.

“Effects of Estrogen on Vascular Function”, February, 2003, *School of Kinesiology and Health Science*, York University, Ontario, Canada.

“Exercise and the Menstrual Cycle: Psychological, sociological, and physiological factors. June, 5, 2003, Keynote for *Society for Menstrual Cycle Research* meeting, Pittsburgh, PA

“Exercise-associated Menstrual Disturbances: Role of Energy Availability”, October 10, 2003. *Faculty of Health and Physical Education*, University of Toronto, Toronto, Ontario, Canada.

“Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction”, November 24, 2003, *Department of Health and Kinesiology, Texas A and M University*, College Station, TX

“Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction”, November 25, 2003, *Department of Nutrition, Texas A and M University*, College Station, TX

“Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction”, December 4, 2003, *Department of Endocrinology, Endocrine Research Conference*, Hershey Medical Center, Penn State University, Hershey, PA

“Exercise-associated menstrual disturbances: Physiological mechanisms and clinical sequelae”, March 2, 2004, Department of Exercise Science, University of Massachusetts, Amherst, MA)

“Exercise-associated menstrual disturbances: Physiological mechanisms and clinical sequelae”, April 30, 2004, Department of Physical Therapy, Faculty of Medicine, University of Toronto, Toronto, Ontario)

“Exercise-associated menstrual cycle disturbances: Physiological and Clinical Considerations”, December, 2004. Department of Exercise Science, University of Connecticut, Storrs, Ct. December, 2004.

Exercise, Estrogen, and Women’s Health: What’s the Connection? Keynote Speaker- Penn State Nutrition Conference, May 13, 2005.

“Estrogen and Cardiovascular Disease”. University of Toronto, Faculty of Physical Education and Health, November 21, 2005.

“The effects of caloric restriction on the menstrual cycle”. Keynote Speaker, Mid-Atlantic American College of Sports Medicine Meeting, Harrisburg, PA November, 2005

SYMPOSIUM PRESENTATIONS DURING THE ENTIRE PERIOD OF SUPPORT BY DAMD17-01-1-0360 (2001-2005)

(TOTAL = 3)

“Menstrual Disturbances in Athletes: Lessons from Prospective Experiments on Animals and Humans (Chairperson Anne B. Loucks, PhD) Lessons from Experimental Disruptions of the Menstrual Cycle in Primates and Humans, N. Williams (*American College of Sports Medicine Annual Meeting*, St. Louis, MO, May 30, 2002)

Chairperson, Symposium on “Current Practices for Screening and Prevention of the Female Athlete Triad” (*American College of Sports Medicine Annual Meeting*, San Francisco, CA, May 31, 2003).

Co-Chairperson, Symposium on “Assessing Endocrine Alterations in Exercising Women”. Weight loss and changes in circulating metabolic hormones and metabolic rate as biomarkers for exercise-associated menstrual disturbances: evidence from prospective studies. Proceedings of the *American College of Sports Medicine Annual Meeting*, Indianapolis, IN, 2004)

CONCLUSIONS:

- Caloric restriction combined with an amount of moderate aerobic exercise shown to be associated with reduced breast cancer risk produces significant weight loss and fat loss in healthy premenopausal women over four menstrual cycles.
- Although previous prospective studies have shown that weight loss can significantly impact menstrual cyclicity and ovarian steroid excretion in young premenopausal women (Bullen, et al. 1985), a exercise and diet stimulus that promotes a similar magnitude of weight loss does not perturb menstrual cyclicity, circulating serum estradiol, estrone, or urinary excretion of estrone -1 -glucuronide (E1G).
- Although previous prospective studies have shown that weight loss can significantly impact menstrual cyclicity and ovarian steroid excretion in young premenopausal women (Bullen, et al. 1985), a exercise and diet stimulus that promotes a similar magnitude of weight loss does not significantly change circulating IGF -1 concentrations.
- The Dried Blood Spot technique represents a viable alternative to determining metabolic status in humans.
- Therefore, these positive lifestyle changes do not appear to reduce breast cancer risk, as it is indicated by these specific circulating biomarkers.

REFERENCES: None

PERSONNEL RECEIVING SUPPORT FROM DAMD17-01-1-0360

Nancy I. Williams, Sc.D.	Principal Investigator 2001-2005
Ann Albert	Project Coordinator 2005
Matthew Johnson	Research Assistant 2005

APPENDIX

NANCY I. WILLIAMS **Curriculum Vitae**

BIOGRAPHICAL

University Address

Department of Kinesiology
Room 108 Noll Laboratory
Penn State University
University Park, PA 16802

Phone: 814-865-1346
Fax: 814-865-1275
Email: niw1@psu.edu

Home Address

1994 North Oak Lane
State College, PA 16803
Phone: 814-231-2021

Citizenship: USA

Date of Birth: 3/13/62

EDUCATION

1984	B.S. Biology, Bucknell University, Lewisburg, PA
1986	M.S. Exercise Physiology, The Ohio State University, Columbus, OH
1992	Sc.D. Applied Anatomy & Physiology, Boston University, Boston, MA
1992-1996	Postdoctoral fellowship, University of Pittsburgh School of Medicine, Center for the Study of Reproductive Physiology (Judy L. Cameron PhD, mentor)

PROFESSIONAL EXPERIENCE

2003-present	<u>Associate Professor</u>	Department of Kinesiology and Noll Physiological Research Center Joint Appointments: Intercollege Program in Physiology, Department of Nutrition, Life Science Consortium (Nutrition Science Option); Penn State University University Park, PA
1997-2003	<u>Assistant Professor</u>	Department of Kinesiology and Noll Physiological Research Center Joint Appointments: Intercollege Program in Physiology, Department of Nutrition, Life Science Consortium (Nutrition Science Option); Penn State University University Park, PA
1996-1997	<u>Visiting Assistant:</u>	Human Anatomy & Physiology

Professor

Department of Biological Sciences
Ohio University
Athens, Ohio

1992-1996 Postdoctoral Fellow: Center for the Study of Reproductive Physiology
School of Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

1987-1992 Graduate Fellow: Department of Health Sciences
Sargent College
Boston University
Boston, Massachusetts

Research Projects: NIH grant: "Effects of exercise on pituitary hormone
secretion"
NIH grant: "Exercise as an adjunct therapy for persons with mental
illness"

Health/Fitness

Center Coordinator:

Faculty/Staff Fitness Program
Department of Health Sciences
Sargent College
Boston University
Boston, Massachusetts

1986-1987 Project Director: Exercise Physiology Laboratory
Department of Exercise Science
The Ohio State University
Columbus, Ohio

NIH Grant: "Effects of chronic exercise training on aging"

1984-1986 Research Assistant: Exercise Physiology Laboratory
Department of Exercise Science
The Ohio State University,
Columbus, Ohio

NIH Grant: "Effects of chronic exercise training on aging"

HONORS AND AWARDS

Canada Research Chair Nomination (declined), York University, Toronto, Ontario, Canada 2003

Department of Defense Breast Cancer Research Program, Career Development Award, 2001

Fellowship Status: American College of Sports Medicine, 1998

NIH Individual National Research Service Award (NRSA), 1994-1996

Endocrine Society; Women in Endocrinology Travel Award, 1995

Association of Women in Science Education Foundation Award, 1990

American Association of University Women Predoctoral Fellowship, 1990

American College of Sports Medicine, New England Chapter Scholarship Award; 1989

Phi Sigma Biological Honor Society; 1984

Scholar/Athlete of the Year, Southern New Jersey Courier Post, 1980

PROFESSIONAL MEMBERSHIPS/AFFILIATIONS

Collaborative Scientist, Oregon National Primate Research Center	2003-present
American College of Sports Medicine	1984-present
Endocrine Society	1996-present
New England Chapter ACSM	1987-1992
Association for Women in Science	1987-1992
Mid-Atlantic Chapter ACSM	1997-present
Female Athlete Triad Coalition	2004-present

TEACHING

COURSES TAUGHT AT BOSTON UNIVERSITY:

HS 276 *Physiology of Exercise Laboratory*
HS 302 *Exercise Physiology (Lecture)*
HS 535 *Clinical Fitness Evaluation*
HS 573 *Physiology of Activity (Lecture)*
HS 573 *Physiology of Activity (Laboratory)*

COURSES TAUGHT AT OHIO UNIVERSITY:

BIOS 450/550 *Principles of Endocrinology (section on neuroendocrinology)*
BIOS 446/546 *Exercise Physiology Laboratory*
BIOS 345 *Human Physiology*
BIOS 346 *Human Physiology Laboratory*

COURSES TAUGHT AT PENN STATE UNIVERSITY:

Sem/Year	Course	Title	Credits	Enrollment
Fall 1997	Kines 481W	Scientific basis of	3	50
		Exercise for Older Adults		
	Kines 496C	Independent Study	3	1
Spring 1998	Kines 456	Fitness Appraisal	4	96
	Kines 496C	Independent Study	3	5
	Kines 395b	Practicum	3	2
Summer 1998	Kines 496C	Independent Study	1-3	3
Fall 1998	Kines 456	Fitness Appraisal	4	86
	Kines 456h	Fitness Appraisal (honors option)*	4	1
	Kines 496c	JumpStart to Health/Fitness	3	6
	Kines 496c	Independent Study	3	5
	Kines 496c	Independent Study (Schreyer Student)**	3	1
	Kines 596c	Supervised Teaching	3	1
	Kines 597i	Neuroendocrine- Immune Interactions	1	4
	Kines 395b	Practicum	3	1
Spring 99	Kines 456	Fitness Appraisal	4	103
	Kines 424	Female in Exercise and Sport	3	36
	Kines 496c	Independent Study	3	16
Summer 99	Kines 456	Fitness Appraisal	4	14
Fall 99	Kines 424	Female in Exercise and Sport	3	16
	Kines 496c	Independent Study**	3	5
	Physio/Bio 572	Animal Physiology	3	12
Spring 00	Kines 456	Fitness Appraisal	4	78
	Kines 424	Female in Exercise and Sport	3	33
	Kines 496c	Independent Study**	3	5
Summer 00	Kines 456	Fitness Appraisal	4	12
Fall 00	Kines 424	Female in Exercise and Sport	3	35
	Physio/Bio 572	Animal Physiology	3	25
	Kines 496c	Independent Study**	3	5
Spring 01	Kines 424	Female in Exercise and Sport	3	35
	Kines 496c	Independent Study**	3	5
Fall 01	Kines 424	Female in Exercise and Sport	3	35
	Kines 496c	Independent Study**	3	5
Fall 02	Kines 424	Female in Exercise and Sport	3	35
Fall 03	Kines 424	Female in Exercise and Sport	3	40
Fall 04	Kines/WMST 424	Female in Exercise and Sport	3	40
Fall 05	Kines/Physio 597d	Estrogen in Physiology and Disease	3	9

*Supervised the writing of new laboratory experiment and handout for Kines 456

** Supervise students who work in my laboratory on research project examining the interactions between reproductive function disturbances, eating habits, and body image

STUDENT TRAINING

Preceptor NIH GM08619-07 Research Training in Physiological Adaptations to Stress. National Institute of General Medical Sciences, 1996-2005. Director is J. Jefferson, Hershey Medical Center, Penn State University

Committee Chair- Undergraduate Honors Thesis Students

- 2000 Kathleen Flecker – Shreyer’s Honor’s College: "Weight and diet concerns among female athletes with menstrual cycle irregularities" (Winner 3rd place Undergraduate Research Exhibition; attended medical school)
- 2003 Meredith Snook- Shreyer’s Honor’s College: “Effects of a diet and exercise on interactions between thyroid hormone, resting metabolic rate, and anthropometric measurements in normal weight healthy young women” (Earned full scholarship to University of Pittsburgh Medical School in a special clinical program designed to train clinicians to conduct clinical research)

Committee Chair- Masters Students

- 1999 Paula Wilkins "Body Image, Social Physique Anxiety, and Menstrual Dysfunction in the Female Athlete" (Physiology)
- 2000 Heather McConnell "Determining the validity of ovulation detection methods in an athletic population" (Physiology)
- 2000 Angelique Matuch "Quantifying physiological responses prior to competitive exercise" (Kinesiology)
- 2002 Megan Senior "Screening for Subclinical Eating Disorders in Female Athletes: The Use of an Indirect Interview Technique " (Nutrition)
- 2004 Michael Perry “ Effects of chemotherapy followed by exercise training on reproductive status and stress hormones in breast cancer patients” (Kinesiology)
- 2004 Kelly Dougherty “No relation between leptin and exercise-associated reproductive disturbances in healthy normal weight young women” (Kinesiology)
- 2004 Brian Frye “Predictors of weight loss in a diet and exercise intervention in young women” (Kinesiology)
- 2005 Sarah Giambuzzi (Kinesiology – In Progress)
- 2005 Jennifer Ward (Physiology- In Progress)

Committee Chair - Doctoral Students

- 1999 *Jill Bush "Proenkephalin peptide F concentrations in different blood bio-compartments: The effect of an acute resistance exercise protocol" (Kinesiology)
*= co-chaired this committee in lieu of the early departure of her major advisor, William Kraemer
- 2004- Heather Leidy “Role of ghrelin in energy homeostasis”(Physiology)

Committee Member- Masters Students

- 1997 Scott Mazetti "The influence of direct supervision of heavy resistance training on muscular performance and hormonal responses" (Kinesiology)
- 1998 Sang Kyung Kim "The effects of menstrual function on plasma peptide F immunoreactivity in response to high intensity cycle exercise" (Kinesiology)

- 1998 Jennifer DeSanto "Body Composition and energy balance: Comparison between eumenorrheic and amenorrheic athletes" (Kinesiology)
- 1998 Wallace Baker "Characterization of leukocyte infiltration after muscle damage" (Kinesiology)
- 1998 Steve Tokeshi "Maximal isokinetic force generation in upper body musculature during concentric and eccentric actions: a gender comparison" (Kinesiology)
- 1999 Jannell MacAulay "Submaximal cycle ergometry as a predictor of maximal aerobic capacity in women on oral contraceptives" (Kinesiology)
- 2000 Brittney Salkeld "The effect of oral contraceptive use on measures of fatigue and energy metabolism" (Kinesiology)
- 2003 James Butler (Media Studies)
- 2003 Micheal Curren "Octreotide improves orthostatic tolerance in women" (Physiology)
- 2005 Rayisa Hontchurak University of Toronto: "Understanding the Female Athlete Triad: A Closer Look at the Components of the Female Athlete Triad and Their Relationships"
- 2005 Dan Lee- University of Toronto : "Metabolic Status and Menstrual Cyclicity in Exercising Women"

Committee Member- Doctoral Students

- 1998 Jeff Volek "Fasting and postprandial serum lipoprotein responses to a hypocaloric low carbohydrate diet rich in monounsaturated fat and supplemented with n-3 fatty acids" (Kinesiology)
- 2002 Greg Daniels "Walking and running: Information and energetics" (Kinesiology)
- 2004-present Stephen Yang (Kinesiology)
- 2005- Nancy Johnston "Bio-markers of pre-term labor" (Nursing)
- 2005-present John Florian (Kinesiology)

Undergraduate Research Advising:

- | | |
|-----------------|--|
| Summer 1998 | Minority High School Student Research Apprentice Program at Penn State University
*Mentored student who helped with research projects in laboratory |
| Fall 98 to 2001 | WISE program; Women in Science in Engineering
*Have averaged two female students per year who have worked in laboratory |
| Summer 2001 | Minority Access to Research Careers (MARC)
*Mentored student who helped with research projects in laboratory |
| Summer 2002 | McNair Scholars Programs
*Mentored first generation college student who performed research project |

RESEARCH

INTRAMURALLY FUNDED GRANTS

(Completed)

1. **Dudley Allen Sargent Research Fund** (intramural): 1988, 1989, 1990
Sargent College of Allied Health Professions
Boston University, Boston, Massachusetts

Principal Investigator:

"Effects of exercise and caloric restriction upon luteinizing hormone secretion"

2. Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program ,

1997-1998;
\$5000

Principal Investigator:

"Prevalence of Female Athlete Triad Disorders: Estimation by Questionnaires and Subsequent Follow-up with Clinical and Laboratory Assessments of Physiological Status"

3. Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program ,

1998-1999;
\$6000

Principal Investigator:

"Disturbances in Reproductive Function caused by Metabolic Stress: Possible Increased Susceptibility in Individuals with Elevated Levels of Perceived Psychological Stress "

4. Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program ,

1999-2000;
\$6000

Co- Investigator: (PI Jay Hertel)

"Changes in risk factors of anterior cruciate ligament ruptures in female collegiate athletes across the menstrual cycle"

5. Penn State University
Pathology Initiation Grant
Hershey Medical Center, Dept. Pathology

January 2002-January 2003 5%
\$15,170

Co-Investigator (PI is Williams' Doctoral student, Thomas Whipple, MS, PT)

"The Role of Resistance Exercise and Energy Availability on Bone

Metabolism"

6. Penn State University
Children's Youth and Family Consortium
Penn State University, CHHD

January 2002- January 2003 5%
\$13, 925

Co-Principal Investigator (with Moira Petit, PhD (PSU-Hershey))

"Designing Intervention Programs to Optimize Bone Development: Application of Bone Markers to Monitor the Short-term Response to Exercise"

EXTRAMURALLY FUNDED GRANTS

(Completed)

1. NIH National Research Service Award (NRSA), 1994-1996

Center for the Study of Reproductive Physiology
School of Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

Principal Investigator:

"Metabolic cues governing reproductive hormone secretion"

2. Pharmavite Corporation, Seattle, Washington

Research Grant-in-Aid, 1998-1999; \$20,000

Principal Investigator:

"Consumer Taste and Education of a Nutritional Sports Supplement"

3. US Army Medical Research and Materiel Command

US Army Breast Cancer Program

1998-2001 5%

\$292,539

Co-Investigator:

"Use of Exercise to Increase CD4 Lymphocytes following Chemotherapy Treatment for Breast Cancer "

4. NIH

1 RO1 HD39245-01 (Williams)

5/1/01 - 4/30/04

30%

PHS/NICHD

\$ 1,538,361

Principal Investigator:

"Bioenergetics of Exercise-induced Menstrual Disturbances"

5. Retirement Research Foundation

2000-2004

2%

\$56,832

Co-Investigator: (PI is J.L. Cameron, PhD)

"Physical Exercise and Brain Aging"

6. Cancer Research and Prevention Foundation

1/04-12/05
\$76,865 0%

"Exercise and Estrogen Metabolism: Implications for Breast Cancer Prevention"

The major goal is to test the hypothesis that a diet and exercise intervention produces favorable alterations in the ratio of key catechol estrogens that are associated with a reduced risk of breast cancer.

Role: Co-Investigator (PI is Kim Westerlind, AMC Cancer Research Center, Denver, CO)

7. Children's Youth and Family Consortium

1/02-1/06

Penn State University, College of Health and Human Development

"Designing Intervention Programs to Optimize Bone Development: Application of Bone Markers to Monitor the Short-term Response to Exercise"

The major goal is to test the hypothesis that acute high impact exercise will produce favorable changes in biochemical markers of bone turnover in young women.

Co-Principal Investigator (PI is Moira Petit, PSU Hershey)

8. US Army Medical Research and Materiel Command

9/17/01- 9/16/05 15%

US Army Breast Cancer Program (IDEA AWARD)

\$408,878

Principal-Investigator:

"Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (IDEA Award) "

9. US Army Medical Research and Materiel Command

9/17/01- 9/16/05 50%

US Army Breast Cancer Program

\$312,081

(CAREER DEVELOPMENT AWARD)

Principal-Investigator:

"Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (Salary Only)

(Funded but Declined)

1. Canada Research Chair, Canada Foundation for Innovation (CFI)

Infrastructure Fund "Research Facility for Reproductive Endocrinology

Fall, 2003
\$220,340 (CDN)

2. Ontario Innovation Trust (OIT)

Ontario Distinguished Researcher Award

Fall, 2003
\$220,340 (CDN)

Active Support

1. PR054531

10/05-10/09

United States Department of Defense CDMRP Program

"Increased Caloric Intake to Reverse Energy Deficiency in Exercising Women: Impact on Bone & Menstrual Cyclicity"

This study investigates the effects of increasing caloric intake in exercising women with reduced bone mass and amenorrhea on menstrual and bone health status.

Role: Co-Principal Investigator (With MJ De Souza)

2. HD-02-012

2003-2008

\$ 1,160,204 5%

NIH Cooperative Reproductive Science Research Centers at Minority Institutions

"The efficacy and safety of metformin and lifestyle factors in the amelioration of Hyperandrogenemia and its associated symptomology"

The major goal is to test the hypothesis that a metformin combined with a lifestyle intervention consisting of diet and exercise resulting weight loss will stimulate the resumption of ovulatory menstrual cycles in adult women with PCOS, and lessen the effects of high circulating androgens in adolescent girls with PCOS.

Role: Co-Investigator

3. NASA

4/1/05-3/31/06

\$1,144,613 5%

"Improving Orthostatic Tolerance in Women: Control of Splanchnic and Cutaneous Vascular Capacitance"

The major goal is to test the hypothesis that increased distribution of blood flow to the splanchnic region contributes to the higher incidence of orthostatic intolerance in women versus men.

Role: Co-Investigator (PI is James Pawelczyk, PSU)

Pending Support:

1. National Institutes of Health (NIH)4/1/05- 3/31/09
\$856,295 15%

“Antioxidant Status, Diet and Early Pregnancy”

Role: Co-Investigator (PI is Terryl Hartmen, Dept. Nutrition, Penn State)

2. **National Institutes of Health (NIH)** 1 RO1 HD39245-01 7/1/05-6/30/09 20%
\$ 2,020,090

“Bioenergetics of Exercise-Induced Menstrual Disturbances”

Role: Principal Investigator

3. **National Athletic Training Association** Research Grant 1/1/06-12/31/06
\$89,113

“Reversing Energy Deficiency in Amenorrheic Athletes: Effects on Bone Turnover and Physical Performance”

Role: Principal Investigator

(Not funded)

1. National Institutes of Health (NIH)1 RO1 (Co –**Principal Investigator** with Mary Jane De Souza, Univ. Toronto)
7/01/02 - 6/30/07 15%
PHS/NICHD \$ 2,433,044
" Clinical Sequelae Exercise-Induced Hypoestrogenism"**2. National Institutes of Health (NIH)****Co-Investigator (PI is Terryl Hartman, PSU)** 4/01/04-3/31/08 20%
\$2,085,448
“Female Cancer Survivors Weight and Activity Intervention”**3. Dairy Farmers of Canada**1/1/05-12/31/06 10%
Co- Principal Investigator (PI is Mary Jane De Souza, University of Toronto)

“Can Increased Dietary Calcium Improve Recovery of Bone Health in Exercising Women Undergoing a Lifestyle Intervention for Severe Menstrual Disturbances?”

4. **National Institutes of Health (NIH)** 4/1/05- 3/31/09 15%
Co-Investigator (PI is Terryl Hartmen, Dept. Nutrition, Penn State) \$856,295

“Antioxidant Status, Diet and Early Pregnancy”

5. National Institutes of Health (NIH)4/1/05-3/31/09 28.8%
Co-Principal Investigator (PI is Susan Bloomfield, Texas A&M)

“Impact of Food Restriction on Bone Health in Active Females

RESEARCH REPORTS TO SPONSORS

Williams NI, Christante DH, Swavely K, Laufer E, McBrearty C, and Clark KC. Penn State Univeristy JogMate Study: Product Effectiveness and Consumer Appeal

Submitted to Pharmavite Corp, Seattle, WA, July 15, 1999

Annual Reports to NIH for

Annual Progress Reports to DAMD for

Annual Progress Reports to DAMD for

PUBLISHED MANUSCRIPTS

1.Skrinar, G.S., **N.I. Williams**, B.A. Bullen, J.W. McArthur, and N.M. Mihok. Changes in body consciousness relate to regularity of exercise training. *Perceptual and Motor Skills*. 75: 696-698, 1992

2.Bloomfield, S.A., **N.I. Williams**, D.R. Lamb, FACSM, and R.D. Jackson. Non-weight bearing exercise may increase lumbar spine bone mineral density in healthy post menopausal women. *Amer. J. Phys. Med. Rehabil.* 72: 204-209, 1993

3.**Williams, N.I.** , J. McArthur, B. Turnbull, B. Bullen, G. Skrinar, I.Z Beitins, G.M. Besser, L.H. Rees, I. Gilbert, D. Cramer, L. Perry, D.S. Tunstall-Pedoe. Effects of follicular phase exercise on LH pulse characteristics in sedentary eumenorrheic women. *Clinical Endocrinology* 41: 787-794, 1994

4.**Williams, N.I.**, J. Young., J. McArthur, B. Bullen, G. Skrinar, and B. Turnbull. Strenuous exercise with caloric restriction: Effect on luteinizing hormone secretion. *Med. Sci. Sports Exerc.* 27 (10): 1390-1398, 1995

5.**Williams, N.I.**, M.J. Lancas, and J.L. Cameron. Stimulation of luteinizing hormone (LH) secretion in male rhesus monkeys by food intake: Evidence against a role for insulin. *Endocrinology* 137(6): 2565-2571, 1996

6.**Williams, N.I.** Low energy availability and reproductive disturbances: a review of clinical and hormonal effects. *Dance Medicine and Science* 2:(1) 19-31, 1998

7.**Williams, N.I.**, B.A. Bullen, J.W. MacArthur, G.S. Skrinar, and B.A. Turnbull. Effects of short-term strenuous endurance exercise upon corpus luteum function”. *Med. Sci. Sports Exerc* 31(7): 949-958,1999.

8.Sharkey, N.A., **Williams, N.I.**, Guerin, J.B.: The role of exercise in the prevention and treatment of osteoporosis and osteoarthritis. *Nursing Clinics of North America*, 35 (1): 209-221, 2000

9. **Williams, N.I.**, Caston-Balderrama, A.L. Helmreich, D.L., Parfitt, D.B., Nosbisch C, Cameron, J.L. Longitudinal changes in reproductive hormones and menstrual cyclicity in cynomolgus monkeys during strenuous exercise training: rapid transition to exercise-induced amenorrhea *Endocrinology* 142: 2381-2389, 2001
10. **Williams NI**, DL Helmreich DL, DB Parfitt, Caston-Balderrama AL, JL Cameron. Evidence for a causal role of low energy availability in the induction of menstrual cycle disturbances during strenuous exercise training. *J Clin Endocrinol Metab* 86: 5184-5193, 2001
11. Miles MP, Mackinnon LT, Grove DS, **Williams NI**, Bush JA, Marx JO, Kraemer WJ, Mastro AM. The relationship of natural killer cell counts, perforin mRNA and CD2 expression to post-exercise natural killer cell activity in humans. *Acta Physiol Scand* 174: 1-9, 2002.
12. McConnell HJ, KA O'Connor, E Brindle, and **NI Williams**. Validity of methods for analyzing urinary steroid data to detect ovulation in athletes. *Med. Sci. Sports Exerc*, 34(11): 1836-1844, 2002
13. Whipple TJ, Petit Moira, Sharkey N, Demers L, **Williams NI**. Leptin and the skeleton. *Clin. Endocrinol.* 57: 701-711, 2002.
14. **Williams, NI**. Experimental disruptions of the menstrual cycle: Lessons from long-term prospective studies. *Med Sci Sports Exerc* 35 (8): 1564-1572, 2003.
15. De Souza, M.J., H. McConnell, E. O'Donnell, B. Lasley, and **Williams NI**. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*J Clin Endocrinol Metab.* Jul;89(7):3536-42, 2004.
16. Leidy HJ, Gardner JK, Frye BR, Snook ML, Schuchert MK, Richard EL, and **Williams NI**. Circulating ghrelin is sensitive to changes in body weight during a diet and exercise program in normal weight young women (Special edition: *J Clin Endocrinol Metab.* Jun;89(6):2659-64, 2004.
17. De Souza, M.J., and **N.I. Williams**. Physiological Aspects and Clinical Sequelae of Energy Deficiency and Hypoestrogenism in Exercising Women (*Hum Reprod Update.* Sep-Oct;10(5):433-48, 2004
18. Whipple TJ, Le BH, Demers LM, Chinchilli VM, Petit MA, Sharkey N, **Williams NI** Acute effects of moderate intensity resistance exercise on bone cell activity *Int J Sports Med.* Oct;25(7):496-501, 2004.
19. De Souza, MJ, **Williams NI**. Beyond Hypoestrogenism in Amenorrheic Athletes: Energy Deficiency As a Contributing Factor for Bone Loss. *Curr Sports Med Rep.* 2005 Feb;4(1):38-44.
20. **Williams, NI** and De Souza, MJ. "Exercise-associated menstrual cycle disturbances: practical and clinical considerations", in "The Endocrine System in Sports and Exercise" as part of the series "The Encyclopedia of Sports Medicine" an International Olympic Committee Medical Commission Publication in collaboration with the International Federation of Sports Medicine. Kraemer WJ, Rogol AD, eds. Blackwell Publishing, Malden, MA, Chp 20, pp 261-278, 2005

21. Hutnick NA, **Williams NI**, Kraemer WJ, Orsega- Smith E, Dixon RH, Bleznak AD, Mastro AM. Exercise and Lymphocyte Activation following Chemotherapy for Breast Cancer Med Sci Sports Exerc. Nov;37(11):1827-1835, 2005.

22. Hertel J, **Williams NI**, Kramer LC, Leidy HJ, Putukian M. Neuromuscular performance and knee laxity do not change across the menstrual cycle of female athletes. (In Press, Knee Surgery, Sports Traumatology, and Arthroscopy, 2005)

23. **Williams NI**, Leidy HJ. Food Attitudes in Female Athletes: Association with Menstrual Cycle Length (*In Press*, Journal of Sport Sciences, 2005)

24. **Williams, NI**. Female Athlete Triad Errors and Misunderstandings. In Press, Medicine, Science, Sports and Exercise, 2006.

MANUSCRIPTS IN REVIEW

1. Leidy HJ, **Williams NI**. Meal energy content affects the meal-related pattern of ghrelin but has no affect on the nocturnal pattern in normal weight, healthy young women (In Review, Hormone and Metabolic Research)

2. De Souza MJ, Hontscharuk R, Olmsted M, Burke, T, Kerr, G, and **Williams NI**. Drive for thinness is a strong predictor of energy deficiency in exercising women (In Review, Physiology and Behavior)

3. **Leidy HJ**, Frye BR, Dougherty, K, Duke KM, Albert AE, Snook ML, **Williams NI**. The Meal Related Pattern and Diurnal Rhythm of Ghrelin are Elevated Following an Energy Deficit-imposing Diet and Exercise Intervention (In Review)

MANUSCRIPTS IN PROGRESS

Williams, N.I. , Berga S.L., and Cameron, J.L. Synergistic effects of multiple stressors on menstrual cyclicity in cynomolgus monkeys. (To be submitted to Journal of Clinical Investigation)

Westerlind KC, Bell J, **Williams, NI**. Effect of Exercise Training on Estrogen Metabolism in Premenopausal Women. (To be submitted to Cancer Epidemiology and Biomarker Prevention)

ABSTRACTS

N.I. Williams, K.A. Greaves, G.R. Brodowicz, T.E. Kirby, and D.R. Lamb, FASCM. Cardiovascular effects of endurance training during submaximal exercise in elders. Exercise Physiology Laboratory, The Ohio State University, Columbus, Ohio, 43210. (research abstract presented at the *Midwest American College of Sports Medicine Winter Meeting*, Boyne Mountain, Michigan, February, 1986)

N.I. Williams, K.A. Greaves, and D.R. Lamb, FACSM. "Cardiovascular function in lean and obese children during acute submaximal exercise". Exercise Physiology Laboratory, The Ohio State University, Columbus, Ohio, 43210. (research abstract presented at the *Midwest American College of Sports Medicine Winter Meeting*, Boyne Mountain, Michigan, February, 1987)

- Williams, N.I.,** K.A. Greaves, T.E. Kirby and D.R. Lamb. Exercise training and cardiovascular function in the elderly. (presented at *Federation for the Society of Experimental Biology* meetings in Washington, DC, 1987) *FASEB Proceedings*, Vol. 46, p. 492, 1987
- Williams, N.I. ,** J. McArthur, B. Turnbull, B. Bullen, G. Skrinar, I. Gilbert, G.M. Besser, and L.H. Rees. Early effects of follicular phase exercise on LH pulse characteristics in sedentary eumenorrheic women. (presented at the *American College of Sports Medicine Annual Meeting, Orlando, FL, May 29-June 1, 1991*) *Med. Sci. Sports Exerc.* 23(4), p. S93, 1991
- Williams, N.I.,** J. McArthur, B. Bullen, G. Skrinar, B. Turnbull, and J. Young. Slowed LH pulse frequency in trained eumenorrheic women due to caloric restriction combined with heavy training. (presented at the *American College of Sports Medicine Annual Meeting, Dallas, TX, May 27-May 30, 1992*) *Med. Sci. Sports Exerc.* 24(5), p. S36, 1992
- Peachey, S., G. Skrinar, E. Kuligowska, B. Bullen, **N. Williams**, B. Turnbull, and J. McArthur. Effect of enhanced follicular phase endurance training on follicular maturation in women. (presented at the *American College of Sports Medicine Annual Meeting, Dallas, TX May 27-May 30, 1992*) *Med. Sci. Sports Exerc.* 24(5), p. S171, 1992
- Skrinar, G.S., D. Hutchinson, and **N. Williams**. Exercise: An adjunct therapy for persons with psychiatric disabilities. (presented at the *American College of Sports Medicine Annual Meeting, Dallas, TX, May 27-May 30, 1992*) *Med. Sci. Sports Exerc.* 24(5), p. S36, 1992
- Bullen, B., B. Turnbull, J. McArthur, G. Skrinar, **N. Williams**, and I. Beitins. Exercise and Diet: Correlates with the onset of menstrual disorders. *Proceedings of the Second IOC World Congress on Sport Sciences*, Barcelona, Spain. p. 155, 1992
- Williams, N.I.,** A.L. Caston, and J.L. Cameron. Induction and reversal of exercise-induced amenorrhea: Temporal correlation with plasma T₃ levels. (presented at the *76th Proceedings of the National Endocrine Society, Anaheim, CA, June, 1994*) *Endocrine Society Abstract*, #1775, 1994
- Williams, N.I.,** M.J. Lancas, and J.L. Cameron. Stimulation of luteinizing hormone (LH) secretion in male rhesus monkeys by food intake: Evidence against a role for insulin. (presented at the *77th Proceedings of the National Endocrine Society, Washington, DC, June, 1995*) *Abstract*, #OR22-3, 1995
- Williams, N.I.,** and J.L. Cameron. Stimulation of luteinizing hormone (LH) secretion in male rhesus monkeys by food intake: Role of circulating triiodothyronine (T₃) (presented at the *10th International Congress of Endocrinology/78th Proceedings of the National Endocrine Society, San Francisco, CA, June, 1996*) *International Congress of Endocrinology/Endocrine Society*, #P2-505, 1996.
- Williams, N.I.,** Berga, S.L., and J.L. Cameron. Mild metabolic stress potentiates the suppressive effect of psychological stress on reproductive function in female cynomolgus monkeys. (presented at the *79th Proceedings of the National Endocrine Society, Minneapolis, MN, June, 1997*) *Endocrine Society Abstract* #P1-367, 1997.
- Williams, N.I.,** Bullen B.A., McArthur J.W., Skrinar G.S., and Turnbull B.A. Effects of short-term strenuous exercise on corpus luteum function. (presented at the *American College of Sports Medicine Annual Meeting, Orlando, FL June 3-6, 1998*) *Med. Sci. Sports Exerc.* 30 (5), p. S324, 1998

- Williams, N.I.** Bullen B.A., McArthur J.W., Skrinar G.S., and Turnbull B.A. Effects of short-term strenuous exercise on corpus luteum function. (presented at the *American College of Sports Medicine Annual Meeting, Orlando, FL June 3-6, 1998 Med. Sci. Sports Exerc.* 30 (5), p. S324, 1998)
- Williams NI**, Clark KL, Mihalko SL, Matuch AN, McConnell HJ. Body image, disordered eating, exercise, and depression in athletes and non-athletes: association with menstrual status. (presented at the *American College of Sports Medicine Annual Meeting, Seattle, WA June 3-6, 1999 Med Sci Sports Exerc* 31(5), S65, 1999)
- Miles MP, Mackinnon LT, **Williams NI**, Bush JA, Marx JO, Mastro AM, Kraemer WJ. NK cell activity and LFA-2 expression after running (presented at the *American College of Sports Medicine Annual Meeting, Seattle, WA June 3-6, 1999*)
- Mackinnon LT, Miles MP, **Williams NI**, Bush JA, Mastro AM. Effects of prolonged exercise on natural killer (NK) cell cytotoxic activity and LFA-2 expression. Book of abstracts. *Fifth IOC World Congress*, Sydney, Australia, Oct 31-Nov 5, 1999, p. 51.
- Mackinnon LT, Miles MP, Grove DS, **Williams NI**, Bush JA, Marx JO, Kraemer WJ. Effects of prolonged exercise on expression of perforin mRNA in peripheral blood natural killer (NK) cells (presented at *Sports Medicine Australia*, 1999)
- Williams NI**, Clark KL, McConnell, Matuch A, O'Connor KA. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up physiological studies (presented at the *American College of Sports Medicine Annual Meeting, Indianapolis, IN, June 3-6, 2000 Med Sci Sports Exerc* 32 (5), S64, 2000)
- Mastro AM, **Williams NI**, et al. Exercise and Recovery of CD4 (+) cells after chemotherapy for breast cancer (presented at *Era of Hope Meeting of US Army Medical Research and Materiel Command*, June 8-12, 2000, Atlanta, GA)
- Flecker KA, **Williams NI**. Body Image, disordered eating and menstrual status in collegiate athletes. (presented at the *National Conference for Undergraduate Research (NCUR)*, University of Montana, Missoula, Montana, April 27-29, 2000)
- Miles MP, MacKinnon LT, Grove DS, **Williams NI**, Bush JA, Marx JO, Kraemer WJ, Mastro AM. Potential mechanisms of post-exercise Suppression of NK cell activity: Cell number, Perforin mRNA and CD2. (research abstract presented at the 2000 American Physiological Society Meeting "The Integrative Biology of Exercise", Portland, ME, September 20-23, 2000.
- Mastro AM, **Williams NI**, Kraemer WJ, Orsega-Smith EM, Perry MD, Dixon RH, Bleznak AD, Underwood J. Exercise, quality of life, and the recovery of CD4 (+) lymphocytes following chemotherapy for breast cancer *Proceedings of the American Association for Cancer Research 92nd Annual Meeting*, New Orleans, LA , 42 : 331, March 24-28, 2001
- Perry MD, Mastro AM, Orsega-Smith E, Miles MP, Kraemer WJ, **Williams NI**. Exercise training and immune function following chemotherapy for breast cancer. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001
- Orsega-Smith E, **Williams NI** (FACSM), Perry MD, Mastro AM, Kraemer WJ, Bleznak A, Dixon R, Underwood J. Fatigue, quality of life and physical function after chemotherapy for breast cancer. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001

- Galucci, AN, **Williams NI**. Physiological indicators of psychological stress prior to competitive exercise. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001
- McConnell HJ, O'Connor KA, Brindle E, **Williams, NI**. Assessing reproductive function in exercising women: validity of ovulation detection algorithms. *Proceedings of the Endocrine Society Annual Meeting*, Abstract #P2-408, 2001
- Senior MK, **Williams NI**, McConnell HJ, Clark KC. Screening for subclinical eating disorders in female athletes: validation of an indirect interview technique. (*Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001*).
- McConnell HJ, **Williams NI**, O'Connor KA, Clark KL, Putukian M. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up clinical and physiological studies. (*Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001*).
- Mastro AM, **Williams NI**, Ford J, Fuener K, Orsega-Smith E, Kraemer WJ, Bleznak AD, Dixon RH, Underwood J, Miles M, Wagner K. IL-6 and interferon-gamma levels following chemotherapy for breast cancer. *Proceedings of the American Association for Cancer Research Annual Meeting*, San Francisco, CA, April 6-10, 2002
- Hertel J, **Williams NI**, Gribble PA, McConnell HJ, DiPasquale AA, Putukian M. Changes in risk factors of ACL injuries across the menstrual cycle: A pilot study. *Proceedings of the American College of Sports Medicine Annual Meeting*, St. Louis, MO, May 29-June 1, 2002
- Williams NI**, McConnell HM, Gardner JK, Albert AC, Cameron JL. Lifestyle factors such as exercise, calories intake, and psychological stress: relationship to reproductive hormones and possibly the risk of breast cancer. *Era of Hope meeting*, Department of Defense Breast Cancer Research Program, Orlando, FL, September 25-28, 2002
- Dougherty, K., Galucci AN, McConnell HJ, **Williams NI**. Cortisol and testosterone levels prior to competitive exercise. *Proceedings of the American College of Sports Medicine Annual Meeting*, San Francisco, May 28-June 1, 2003, *Med. Sci. Sports Exerc.* 35 (5), p. S1837, 2003.
- Williams NI**, McConnell HJ, Gardner JK, Cameron JL, Schuchert MK, Richard EL, Snook ML. Susceptibility of menstrual cycle to various stressors: correlation with baseline luteal progesterone levels. *Proceedings of the American College of Sports Medicine Annual Meeting*, San Francisco, May 28-June 1, 2003, *Med. Sci. Sports Exerc.* 35 (5), p. S12, 2003.
- McConnell HJ, Schuchert MK, Gardner JK, Frye BR, **Williams NI**. Basal Ghrelin is sensitive to changes in body weight during a controlled diet and exercise program in normal weight young women. (*Presented at the 2003 Endocrine Society Meeting, Philadelphia, PA, June 2003*).
- Whipple TJ, Le, B., Demers, L., Petit M.A., Sharkey N. **Williams, NI**. Acute Effects of Moderate Intensity Resistance Exercise on Bone Cell Activity. (*Presented at Association for Bone and Mineral Research Meeting, 2003*).

- J K Gardner, H J McConnell, B R Frye, K A Dougherty, T S Parrott, E L Richard, M L Snook, M Schukert, **Williams, NI**. Validation of an Improved Method to Estimate Energy Requirements in College-aged Women: The PERK method (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S79, 2004)
- K Dougherty , H J McConnell, J Gardner, B Frye, E Richard, M Snook, M Schucert, A Albert, T Parrott and **Williams, NI**. Effects of Diet and Exercise on Leptin Levels In Women: Dependence on Body Composition Changes (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S80, 2004)
- Williams, NI**, HJ McConnell, JK Gardner, BR Frye, EL Richard, ML Snook, KL Dougherty, TS Parrott, A Albert, M. Schukert. Exercise-associated menstrual disturbances: dependence on daily energy deficit, not body composition or body weight changes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.
- De Souza, M.J., E. O'Donnell, R. Hontscharuk, T. Burke, J. Goodman, **Williams, NI**. Diagnosis of Osteopenia May Indicate the Presence of Increased Cardiovascular Risk in Female Athletes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.
- R. Hontscharuk, E. O'Donnell, **Williams, NI** T. Burke, M.J. De Souza. Dietary Cognitive Restraint: A Marker for Altered Energy Homeostasis and Menstrual Disturbances in Athletic Women (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S33, 2004.
- McConnell, H., **Williams, NI**, E. O'Donnell, B. Lasley, M.J. De Souza. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004)
- De Souza MJ, Lee D, Burke T, Hontscharuk R, O'Donnell E, Williams NI. Metabolic Adjustments to Maintain Energy Balance in Amenorrheic Exercising Women Indicate Chronic Energy Deficiency. (Abstract # P3-568, Proceedings of Endocrine Society, San Diego, CA, 2005) p. 684.
- Williams NI**. Leidy HJ, Legro R, Demers L, Gardner J, Frye B, Dougherty K, Albert A, Parrott T, De Souza MJ. Predictors of Menstrual Disturbances in Exercising Women. (Abstract # P3-569, Proceedings of Endocrine Society, San Diego, CA, 2005) p. 684.
- Williams NI**, Albert AC, Parrott TS, Leidy HJ, Frye B, Snook M, Duke, KA, Richard EL, Gardner JK. Effects of caloric restriction combined with moderate aerobic exercise on circulating estrogens and IGF-I in premenopausal women. (Abstract presented at 2005 Era of Hope Breast Cancer Research Meeting, Philadelphia, PA, June, 2005)
- A.M. Mastro, N.A. Hutnick, **N.I. Williams**, W.J. Kraemer, E. Orsega-Smith, R.H.Dixon, A.D. Bleznak. The use of exercise to increase lymphocyte activation following chemotherapy for breast cancer. (Abstract presented at 2005 Era of Hope Breast Cancer Research Meeting, Philadelphia, PA, June, 2005)

Kim C. Westerlind, Jennifer Bell, and **Nancy I. Williams**, Estrogen Metabolism is Altered with Exercise Training (Submitted for presentation at 2006 American College of Sports Medicine Meeting, Denver, Colorado, 2006)

Brandy Weller, Ann Albert, Matthew Johnson, and **Nancy I. Williams** Susceptibility to energy-related menstrual disturbances is reduced with increased age. (Submitted for presentation at 2006 American College of Sports Medicine Meeting, Denver, Colorado, 2006)

Jennifer L. Scheid, **Nancy I. Williams**, Sarah L. West Tanya G. Burke, Mary Jane De Souza. Bone Resorption Is Increased In Premenopausal Exercising Women With Osteopenia (Submitted for presentation at 2006 International Osteoporosis Federation, June 2006, Toronto, Ontario, Canada)

INVITED PRESENTATIONS

"Cardiovascular/Medical Applications for Aerobic Exercise", *Aerobics and Fitness Association of America (AFAA), National Primary Certification Workshop*, Boston, Massachusetts, October 3, 1987.

"Principles and Benefits of Exercise Training for Seniors", *Annual Health Program, Leo Yassenoff Jewish Community Center*, Columbus, Ohio, June 6, 1987.

"ACSM Certification, Tracts Offered and Benefits Provided", *American College of Sports Medicine, New England Chapter Annual Meeting*, Worcester, Massachusetts, November 2-3, 1989.

"Special Topics for Students", *American College of Sports Medicine, New England Chapter Annual Meeting*, Worcester, Massachusetts, November 2-3, 1989.

"Exercise Testing and Prescription", *Harvard Medical School Department of Continuing Education Conference: "Current Advances in Nutritional Medicine and Disease Prevention: Medical Treatment Strategies"*, Boston, Massachusetts, April 25, 1991

"Eating Disorders and Body Image With Special Emphasis on the Female Athlete", *New York State Association of Physician's Assistants*, Calicoon, NY, April 18, 1998.

"Exercise and Female Hormones: What are the Health Risks and Benefits?" *American College of Sports Medicine Health Fitness Summit*, April 14-18, 1999, New Orleans, LA

"Women's Health and Fitness Issues" *Panel Discussion at American College of Sports Medicine Health Fitness Summit*, April 14-18, 1999, New Orleans, LA

"Modulation of Reproductive Function by Metabolic Cues", invited speaker for *Bucknell University Biology Department Seminar Series*, March 3, 2000. Bucknell University, Lewisburg, PA

"Career Development for Women" *Women and Sciences and Engineering (WISE) program* for potential college students from surrounding area and other states, June 19, 2000, Penn State University

"Low Energy Availability and the Menstrual Cycle: Clinical and Physiological Implications" *Society for the Study of the Menstrual Cycle, Bi-Annual meeting*, June, 2001, Hartford Connecticut

"Physiological Connections Between Factors of the Female Athlete Triad" *Penn State Athletic Training Conference*", April 12, 2002, Penn State University, University Park, PA

"Exercise and Women's Health: Lessons from the Female Athlete Triad", Department of Health and Exercise Science, April 25, 2002, *Wake Forest University*, Winston-Salem, NC

"Subclinical Eating Disorders and Menstrual Cycle Irregularities in Female Athletes" *Eating Disorders on Campus, The Institutional Response*, June 7, 2002, Eighth Annual Conference, Penn State Conference Center Hotel, Penn State University, University Park, PA

"Effects of Exercise on the Menstrual Cycle: Physiological mechanisms and practical considerations" February, 2003, *School of Kinesiology and Health Science*, York University, Ontario, Canada.

"Effects of Estrogen on Vascular Function", February, 2003, *School of Kinesiology and Health Science*, York University, Ontario, Canada.

"Exercise and the Menstrual Cycle: Psychological, sociological, and physiological factors. June, 5, 2003, Keynote for *Society for Menstrual Cycle Research* meeting, Pittsburgh, PA

"Exercise-associated Menstrual Disturbances: Role of Energy Availability", October 10, 2003. *Faculty of Health and Physical Education*, University of Toronto, Toronto, Ontario, Canada.

"Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction", November 24, 2003, *Department of Health and Kinesiology, Texas A and M University*, College Station, TX

"Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction", November 25, 2003, *Department of Nutrition, Texas A and M University*, College Station, TX

"Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction", December 4, 2003, *Department of Endocrinology, Endocrine Research Conference*, Hershey Medical Center, Penn State University, Hershey, PA

"Exercise-associated menstrual disturbances: Physiological mechanisms and clinical sequelae", March 2, 2004, Department of Exercise Science, University of Massachusetts, Amherst, MA)

"Exercise-associated menstrual disturbances: Physiological mechanisms and clinical sequelae", April 30, 2004, Department of Physical Therapy, Faculty of Medicine, University of Toronto, Toronto, Ontario)

"Exercise-associated menstrual cycle disturbances: Physiological and Clinical Considerations", December, 2004. Department of Exercise Science, University of Connecticut, Storrs, Ct. December, 2004.

Exercise, Estrogen, and Women's Health: What's the Connection? Keynote Speaker- Penn State Nutrition Conference, May 13, 2005.

"Estrogen and Cardiovascular Disease". University of Toronto, Faculty of Physical Education and Health, November 21, 2005.

“The effects of caloric restriction on the menstrual cycle”. Keynote Speaker, Mid-Atlantic American College of Sports Medicine Meeting, Harrisburg, PA November, 2005

SYMPOSIUM PRESENTATIONS

Chairperson, Symposium on "Special Topics of Interest to Students in ACSM", *American College of Sports Medicine, New England Chapter Annual Meeting*, Worcester, Massachusetts, November 2-3, 1989.

“Menstrual Disturbances in Athletes: Lessons from Prospective Experiments on Animals and Humans (Chairperson Anne B. Loucks, PhD) Lessons from Experimental Disruptions of the Menstrual Cycle in Primates and Humans, N. Williams (*American College of Sports Medicine Annual Meeting*, St. Louis, MO, May 30, 2002)

Chairperson, Symposium on “Current Practices for Screening and Prevention of the Female Athlete Triad” (*American College of Sports Medicine Annual Meeting*, San Francisco, CA, May 31, 2003).

Co-Chairperson, Symposium on “Assessing Endocrine Alterations in Exercising Women”. Weight loss and changes in circulating metabolic hormones and metabolic rate as biomarkers for exercise-associated menstrual disturbances: evidence from prospective studies. Proceedings of the *American College of Sports Medicine Annual Meeting*, Indianapolis, IN, 2004)

WORKSHOPS ATTENDED

The X and Y: Current Topics in Gender – Specific Medicine, April 6-7, 2001
Harvard Medical School, Department of Continuing Education, Boston, Massachusetts

SERVICE

PROFESSIONAL SERVICE

COMMITTEES

American College of Sports Medicine Student Affairs Committee,
Student Representative for New England Chapter, 1988-1990

American College of Sports Medicine Executive Committee,
Member at Large, New England Chapter, 1990-1991

American College of Sports Medicine, Strategic Health Initiative Committee: Women, Sports and Physical Activity, June 2000-2002

American College of Sports Medicine, Credentials Committee, Spring 2003-present

American College of Sports Medicine, Position Stand Review Committee, “Female Athlete Triad,” Spring 2002-present

REVIEWER

Journals	<i>Journal of Applied Physiology, ACSM Health Fitness Journal Medicine, Science, Sports and Exercise, Journal Clinical Endocrinology and Metabolism</i>
Grants	Dissertation Awards, Susan B. Komen Foundation for Breast Cancer Research (2001-2002)
Editorial Board	American College of Sports Medicine <i>Health and Fitness Journal</i> (2002-present)

Fellow American College of Sports Medicine, June, 1998

Participant "Biopsychology of Infertility Workshop"
Sponsored by National Institutes of Health (National Institute of Child
Health and Human Development); September 21-22, 1995; NIH Campus,
Bethesda, Maryland

UNIVERSITY SERVICE

Advisory Board: The Tremin Trust Research Program on Women's Health, Penn State University,
University Park, PA, 2001-present

COLLEGE SERVICE

Presenter: College of Health and Human Development, Development Council Retreat. October 15-17, 20004,
Westin Grand Hotel, Washington, DC.

University Committees

Faculty Senate (Spring 2002)-Senate Committee on Intra-University Relations

College Committees and Service (College of Health and Human Development)

College of Health and Human Development Seed Grant Review Committee (Fall 00)
Faculty Council (Fall 00- Spring 2001)
Presentation to Alumni Council at Annual Alumni Council Retreat, Washington DC, October, 2004
Women's Leadership Initiative- Fall 05

Intercollege Program Committee (Physiology)

Candidacy Exam Committee (Intercollege Program in Physiology) (Spring 01-present)

Department Committees (Department of Kinesiology)

Curriculum Committee	Fall, 1998 to Spring 2002
Candidacy Committee	Fall, 1998 to 2002
Search Committee	Fall, 1998
(Noll Laboratory Exercise Physiology positions)	
Search Committee	Spring 99
(General Education Fitness Position)	
Search Committee	Fall 01-Spring 02
(Department of Kinesiology Chair)	

Curriculum Revisions (ad hoc)	Spring 01-Spring 02
Advisory Committee for Fitness Assessment Program	Spring 02-present
Search Committee (Director, Noll Laboratory)	Fall 02-Spring 04)
Advisory Committee	Fall 02-present
Search Committee (Pedagogy Positions)	Spring 2003-present
Search Committee (Noll Endowed Professorship)	Summer 04-present
Promotion and Tenure Committee	Fall 04-Spring 05
Promotion and Tenure Committee (Chair)	Fall 05-present
Search Committee (Chair)	December, 2005
(Kinesiology Assistant Professor in Exercise Psychology)	

University Presentations

Fall 1997	Kinesiology Proseminar	“Professional Development”
Fall 1998	Kinesiology Proseminar	“Professional Development”
Fall 1997	Nutrition Ingestive Behavior Journal Club	“Reproductive disturbances and low energy availability: aberrant eating habits”
Fall 1997	Kinesiology Colloquium	“Low energy availability and the female athlete: Clinical and Hormonal Effects”
Fall 1997	Population Research Institute	“Modulation of Reproductive Function by Metabolic Cues”
Spring 1998	Nutrition Dept. Colloquium	“Modulation of Reproductive Function by Metabolic Cues”
Spring 1998	Biobehavioral Health Dept. Colloquium	“Reproductive disturbances caused by low energy availability: Interaction with psychological stressors”

OTHER SERVICE

News article, Kinesiology Today, Spring 1999 issue, “Study links Body Image to Athletes’ Fertility”

Interview/article, The Penn Stater, September/October 1999 issue “Research and Discovery Section” by Nick McCarthy

Interview/article, The Penn Stater, 2000 issue of undergraduate research, “Research and Discovery”

Interview/article, Intercom, July, 1999. featured in “Focus on Research” article, by Barbara Hale.

2000 Undergraduate Exhibition

Served as Judge for the 2000 Undergraduate Exhibition in April, 2000.